PUBLIC HEALTH PAPERS 42

THE PREVENTION OF PERINATAL MORBIDITY AND MORTALITY

Report on a Seminar

WORLD HEALTH ORGANIZATION
GENEVA

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No. 42

THE PREVENTION OF PERINATAL MORBIDITY AND MORTALITY

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THE PREVENTION OF PERINATAL MORBIDITY AND MORTALITY

Report on a Seminar

Tours, 22-26 April 1969

WORLD HEALTH ORGANIZATION

GENEVA

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PREFACE

WHO has convened a number of meetings to consider problems related to the prevention of perinatal morbidity and mortality. Following these meetings, a Seminar was organized at Tours with the following aims:

(a) to analyse perinatal mortality in order to bring out factors that stand in the way of a more substantial reduction;

(b) to review the theoretical and practical aspects of certain medical problems, concerning which important new facts have come to light in recent years;

(c) to rethink the organization of the care available to the pregnant woman and newborn infant, particularly preventive care;

(d) to study the changes that need to be made in medical education at all levels in the light of new medico-social knowledge about maternal and child health.

The subject is a topical one, but stress is laid on the difficulties involved in devising a rational prevention plan in the face of the enormous gaps in knowledge of some quite common medical problems (pathogenesis and physiopathology of antepartum haemorrhage and toxaemia of pregnancy, causes of premature birth or prolonged gestation, mechanisms responsible for hyaline membrane disease and for the recurrent apnoea syndrome in the child born before term, etc.). The lack of epidemiological data on perinatal morbidity that cover an entire region rather than a non-representative hospital population has been keenly felt, as has the ineffectiveness of present measures to prevent congenital malformations and hereditary metabolic diseases. These gaps in medical knowledge indicate the direction that research should take in future years.

The Seminar was attended by 45 participants from 29 countries of the European Region, a consultant, 12 temporary advisers, and representatives of WHO headquarters and the Regional Office. A number of observers and representatives of non-governmental organizations were also present.

The participants were welcomed by Professor P. Boulenge, Director-General of Public Health, and by Mr A. Dubois-Chabert, Prefect of Indre-et-Loire. The meeting was opened on behalf of the Regional Director for Europe, Dr Leo A. Kaprio, by Dr A. C. Eberwein, Chief, Health Protection and Promotion.

Dr L. S. Prod'hom, University Paediatrics Department, Cantonal Hospital, Lausanne (Switzerland), acted as rapporteur. Small groups were formed to discuss certain topics in depth, and their conclusions were presented at plenary sessions.

INTRODUCTION

In most countries of the WHO European Region, perinatal and infant mortality declined between 1956 and 1966, a phenomenon that was closely associated with socio-economic progress and improvements in the basic health and social services. Infant mortality fell more rapidly than did perinatal mortality, and the decline in infant mortality was particularly marked between one month and the end of the first year of life. This may be accounted for mainly by the success of the measures taken to improve health care and reduce the risk of infections and by better infant feeding. To achieve a reduction in perinatal mortality, however, it is not sufficient merely to improve environmental conditions; there are more fundamental phenomena, such as the constitution of the mother and the genetic characteristics of the fetus and the newborn, to be considered, but these are difficult to influence.

The problems of improving the survival prospects at birth may be considered to have both a quantitative aspect—reduction in the number of perinatal deaths—and a qualitative one—survival of the newborn under optimal conditions. Thanks to the progress that is being made in obstetric and paediatric care, infants now survive who would formerly have been lost because of malformations or complications present at birth (fetal growth anomalies, asphyxia, respiratory distress, metabolic disorders, etc.). The qualitative aspect of survival is therefore becoming more and more important, from both the medical and the public health points of view.

CHAPTER 1

EPIDEMIOLOGICAL AND STATISTICAL DATA

ANALYSIS OF PERINATAL MORTALITY

Perinatal mortality recorded in twenty-five countries of the WHO European Region in 1966 (Table 1) lies within a relatively narrow range, varying from 19.0 to 43.6 per 1000 live births. Fig. 1 shows the same data in order of increasing size and broken down into late fetal and early neonatal deaths. The relative sizes of these two subgroups vary significantly: for example, Finland and Czechoslovakia have very similar rates for perinatal mortality as a whole, but the ratio of first-week deaths to late fetal deaths in Czechoslovakia (1: 1.8) is nearly twice that in Finland (1: 1). Perinatal and infant mortality generally show similar trends (Table 2), though there are exceptions, for example in Bulgaria and Romania. Such differences, which are often considerable, cannot be understood without studying the way in which the statistics are collected and the medico-social practices of the countries concerned.

Registration practices

Registrations of late fetal deaths show marked variations from one country to another. The "viability" criteria,[1] which set the lower limit for late fetal death and distinguish it from abortion, may be based on size (30 cm in Switzerland, 35 cm in Austria and the Federal Republic of Germany), on weight (1000 g in Poland), on both size and weight (Finland: length 25 cm, weight 600 g), or on duration of gestation. In Belgium, France, Morocco and Monaco, a late fetal death is defined as one occurring after 180 days of gestation, whereas, according to a

[1] Butler, R.N. (1966) *The causes and prevention of perinatal mortality in the European Region* (Unpublished working document EUR/RC16/Techn.Disc./1).

TABLE 1. SOME STATISTICAL DATA ON LIVE BIRTHS, INFANT MORTALITY AND PERINATAL MORTALITY FOR THE YEAR 1966

Country	Population in mid-1966 (in thousands)	Number of live births per 1 000 population	Number of perinatal deaths per 1 000 live births	Number of late fetal deaths per 1 000 live births	Number of first-week deaths per 1 000 live births	Number of first-day deaths per 1 000 live births	Number of first-year deaths per 1 000 live births
Albania	1 914	34.0	...	...	...	...	86.3 [a]
Algeria	12 148	...	...	...	...	...	...
Austria	7 290	17.6	29.8	11.4	18.4	11.6	28.1
Belgium	9 528	*15.8	27.3 [a]	13.4	13.9 [a]	8.0 [a]	*25.5
Bulgaria	8 257	14.9	19.0	9.9	9.1	1.8	32.2
Czechoslovakia	*14 240	15.6	22.8 [a]	8.1	14.6 [a]	9.0 [a]	*23.7
Denmark	4 797	18.4	21.8	9.9	11.9 [b]	4.6 [a,b]	16.9
Federal Republic of Germany	57 485	17.8	27.9	11.6	16.3	9.1 [a]	23.5
Finland	*4 637	*16.8	20.8 [a]	10.3	10.5	5.9 [a]	15.0
France	*49 400	*17.5	27.7	15.2	12.5	2.0 [a,b,c]	*21.7
German Democratic Republic	15 988	15.8	25.5	12.7	12.8 [a]	*9.1 [a]	23.2
Greece	8 614	17.9	30.4	15.9	14.5	5.2	34.0
Hungary	10 179	13.6	35.3	10.9	24.4	13.9	38.4
Iceland	196	23.9	20.8	12.2	8.6	3.9	13.7
Ireland	2 884	21.6	29.1	16.0	13.1	7.3 [b]	24.9 [b,c]
Italy	51 962	18.9	36.8 [a]	19.7 [d]	17.1 [a]	8.6 [a]	34.3
Luxembourg	335	15.5	23.3	10.8	12.5	6.9	26.8
Malta and Gozo	317	16.8	32.4	12.4	20.0	12.5	30.1
Monaco	23	21.4	...	8.1	...	...	10.1
Morocco	13 725	...	...	...	...	...	...
Netherlands	12 455	19.2	22.7	13.1	9.6 [d]	4.3 [d]	14.7 [d]
Norway	*3 753	*17.9	21.1	12.1	9.0	4.1 [a]	16.8 [a]
Poland	31 698	16.7	25.1 [a]	10.9	13.8 [a]	6.6 [a]	38.8

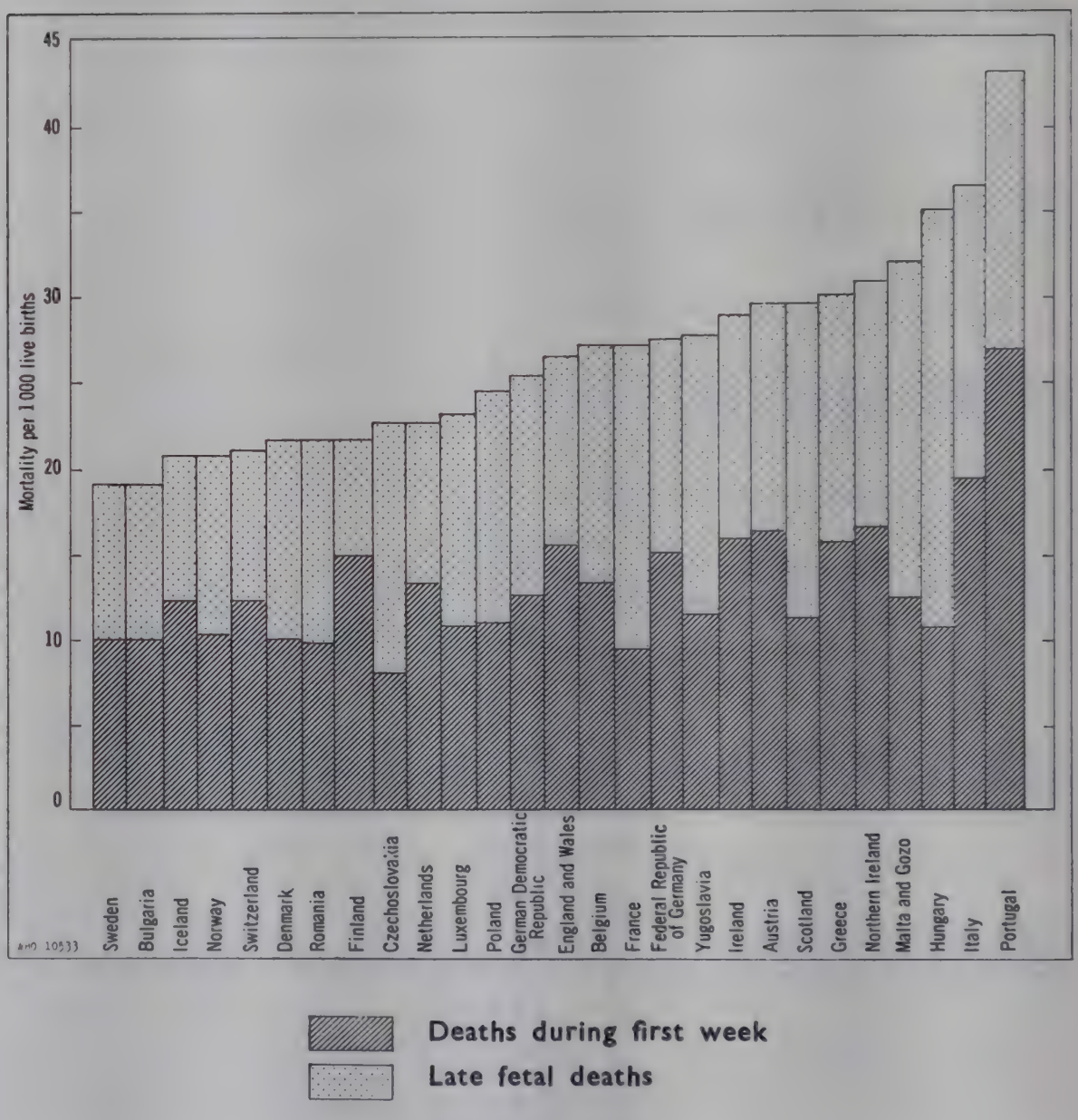
Portugal	9 335	22.2	43.6	27.3	16.3	8.1	64.7
Romania	19 143	14.3	21.9	14.9	7.0	1.2	46.6
Spain	31 871	*20.9	...	21.3	...	9.4	*34.6
Sweden	7 808	*15.8	18.9	10.0	8.9	4.0	12.6
Switzerland	5 999	*18.3	21.7	10.0	11.7	8.0[a]	17.8[a]
Turkey	31 910	...	...	...	...	...	161[e]
United Kingdom							
England and Wales	48 075	17.7	26.7	15.6	11.1[b]	*6.5[b]	*19.0[f]
Northern Ireland	1 478	22.3	31.3	16.6	14.7[b]	9.1[b]	25.6[g]
Scotland	5 191	18.6	29.8	16.4	13.3[b]	7.9[b]	23.2[g]
USSR	233 105	18.2	...	...	...	...	26.1
Yugoslavia	19 735	20.2	27.4[a]	9.4	18.0	6.5	*61.3

Sources: World Health Statistics Report, 1969, **22**, No. 1; United Nations Demographic Yearbook, 1967.

* Provisional data.
[a] Data for 1965.
[b] Data tabulated by year of registration and not by occurrence.
[c] Data exclude liveborn children who died before their birth was registered.
[d] Including fetal deaths occurring after the 180th day of gestation (6 calendar months or 26 weeks).
[e] Estimate based on incomplete returns of the Turkish Demographic Survey.
[f] Data tabulated by year of occurrence.
[g] Data tabulated by year of registration.

WHO recommendation (Annex 1), the minimum period of gestation is 28 full weeks counting from the first day of the last menstrual period. The WHO recommendation has been adopted in Bulgaria, Denmark, Greece, Hungary, Ireland, Italy, Malta, the Netherlands, Norway,

FIG. 1. PERINATAL MORTALITY RATES IN EUROPE, 1966



Portugal, Romania, Sweden, and the United Kingdom. In some countries, both duration of gestation and size of the fetus are taken as criteria (Albania and Iceland: 28 weeks, 35 cm), in others duration of gestation and weight (Czechoslovakia and Yugoslavia: 28 weeks, 1000 g), and in still others, duration of gestation, length and weight (USSR: 28 weeks, 35 cm, 1000 g). Finally, in some countries, such as Spain, there are no criteria at all.

TABLE 2. PERINATAL MORTALITY, LATE FETAL MORTALITY, EARLY NEONATAL MORTALITY, AND MORTALITY FROM ONE WEEK TO 11 MONTHS IN THE WHO EUROPEAN REGION IN 1956 AND 1966, WITH THE PERCENTAGE CHANGE

Country	Perinatal deaths per 1 000 live births			Late fetal deaths per 1 000 live births			Deaths in first week per 1 000 live births			Deaths from one week to 11 months per 1 000 live births		
	1956	1966	% change	1956	1966	% change	1956	1966	% change	1956	1966	% change
Austria	40.3	29.8	— 26.1	18.0	11.4	— 36.7	22.3	18.4	— 17.5	21.0	9.7	— 53.8
Belgium	35.1	27.7 [a]	— 21.1	17.0	13.4 [a]	— 27.1	16.9	14.0 [a]	— 18.0	21.3	9.8 [a]	— 10.8
Bulgaria	—	19.0	—	—	9.9	—	16.2	9.1	— 43.8	55.8	23.1	— 58.6
Czechoslovakia	22.5	22.8 [a]	+ 1.3	11.2	8.2 [a]	— 26.8	11.3	14.6 [a]	+ 29.2	20.1	10.9 [a]	— 45.8
Denmark	33.0	21.9	— 33.6	17.8	9.9	— 44.4	15.3	11.9	— 22.2	9.6	5.0	— 47.9
Federal Republic of Germany	40.1	27.9	— 30.4	18.8	11.6	— 38.3	21.3	16.3	— 23.5	16.6	7.3	— 56.0
Finland	29.2	20.8	— 28.8	15.3	10.3	— 32.7	13.8	10.5	— 23.9	11.8	4.5	— 61.9
France	33.8	27.7	— 18.8	17.5	15.2	— 13.1	16.3	12.5	— 23.3	19.9	9.3	— 53.3
Greece	—	30.4	—	—	15.9	—	10.5	14.5	+ 38.1	28.2	19.5	— 30.9
Hungary	38.1	35.5	— 7.3	15.8	10.9	— 31.0	22.3	24.4	+ 9.4	36.5	14.0	— 61.6
Iceland	—	20.8	—	—	12.2	—	9.4	8.6	— 8.5	8.1 [b]	5.1	— 37.0
Ireland	—	29.1	—	—	16.0	—	15.7	13.1	— 16.6	19.9	11.8	— 40.7
Italy	45.4	36.2 [a]	— 20.3	26.6	19.7 [a]	— 25.9	18.8	17.1 [a]	— 9.0	29.9	18.5 [a]	— 38.0
Malta	—	—	—	—	12.4	—	20.0	20.0	0.0	22.6	10.1	— 55.3
Netherlands	28.3	22.7	— 19.8	17.2	13.1	— 23.8	11.1	9.6	— 15.3	7.9	5.1	— 35.4
Norway	25.9	21.6 [a]	— 18.5	15.4	11.0 [a]	— 28.7	10.5	10.6 [a]	+ 1.0	10.7	6.2 [a]	— 42.0
Poland	—	25.1 [a]	—	—	11.3 [a]	—	18.4	13.8 [a]	— 25.0	52.3	27.9 [a]	— 46.7
Portugal	49.9	43.6	— 12.6	34.2	27.3	— 20.2	15.6	16.3	+ 4.5	72.2	48.4	— 33.0
Romania	—	21.9	—	—	14.9	—	12.9	7.0	— 45.7	68.6	39.6	— 42.3
Sweden	28.8	19.0	— 34.0	17.0	10.0	— 41.2	11.7	8.8	— 23.9	5.6	3.7	— 33.9
Switzerland	30.2	23.1 [a]	— 23.5	13.7	10.6 [a]	— 22.7	16.5	12.5 [a]	— 23.2	9.3	5.3 [a]	— 43.0
United Kingdom												
England and Wales	37.6	26.7	— 29.0	23.4	15.6	— 33.3	14.1	11.1	— 21.3	9.4	7.9	— 16.0
Northern Ireland	—	31.3	—	—	16.6	—	17.3	14.7	— 15.0	11.5	10.9	— 5.2
Scotland	40.7	29.8	— 26.8	24.4	16.4	— 32.8	16.3	13.3	— 18.4	12.3	9.9	— 19.5
Yugoslavia	—	27.8	—	—	9.4	—	19.5	18.0	— 7.7	78.8	43.3 [b]	— 45.1

[a] Data relating to 1965.
[b] Provisional data.

A similar diversity is found in the criteria of "signs of life". Here, again, the WHO definition (Annex 1) is not uniformly applied. The differences in the criteria used to establish the presence or absence of life do not affect perinatal mortality data as a whole, but only the relation between late fetal and early neonatal mortality. Thus, in Czechoslovakia strict application of the WHO definitions has resulted in a very low late fetal mortality (8.1 per 1000 live births) with a relatively high perinatal mortality (22.8 per 1000).

Moreover, in some countries, the newborn are recorded as live only if they survive the first twenty-four hours (for example, in Poland) or if they are still alive when the birth is officially registered (Algeria, France, Greece, Luxembourg, Morocco, and Spain). This practice swells the number of late fetal deaths in relation to early neonatal deaths.

The wide variations in the registration of late fetal deaths and live births described above make any intercountry comparison of statistics difficult, if not futile.

Medico-social practices

Some countries, such as Bulgaria and Romania, have fairly low perinatal mortality rates, although late infant mortality there is still considerable. These countries practise or have practised interruption of pregnancy on a large scale (Potts, 1967). Many of these abortions are authorized for medico-social reasons: poor health, advanced age of the mother, high parity, unmarried mother, inadequate housing, financial difficulties, and so on—situations often associated with perinatal deaths. Consequently, legal abortions performed during the first weeks of pregnancy, undoubtedly eliminate many fetuses that would later have been particularly at risk.

Causes of death

The interpretation of certified causes of perinatal death is often extremely difficult. In most cases, the principal cause of death can be found only by a thorough pathological examination to detect cerebral lesions, internal malformations, and so on. The placenta should also be examined for the presence of placental infarcts, etc.

Czechoslovakia is the only country in the European Region that gives exact information on causes of death (proportion of deaths in which autopsies are performed: 75% to 91% in different years), thus making it possible to assess changes in perinatal pathology over a long period. Of the stated causes, birth weight is the simplest, and it is interesting to note that in 1959, with a perinatal mortality of 21.9 per

1000, 56.5% of the infants that died weighed less than 2500 g, whereas in 1965, with a rate of 22.8 per 1000, 68.7% of the deaths were in fetuses and newborn of less than 2500 g. The proportion of deaths caused by intrauterine asphyxia, malformations and antenatal infections remained stationary. On the other hand, intracranial and spinal injuries at birth, postnatal infections and haemolytic disease of the newborn declined, while the proportion of deaths due to neonatal lung diseases increased. This study shows the importance of low birth weight and hypoxia (antenatal asphyxia, cerebral injuries, neonatal lung diseases) as causes of death.

In the absence of pathological examination, analysis of the certified causes of deaths reveals a very great variety in the diagnoses reported. The differences relate not only to registration practices, but also to the methods of selecting and coding (according to the International Classification of Diseases) the underlying cause of death, which is often multifactorial and may be associated with the mother, the placenta or the fetus. For this reason, it would be worth while considering the advantages of introducing a special perinatal death certificate, which would also make it possible to obtain a wider range of information (see the draft proposals of the United Nations, Annex 2). Such a certificate is already being used in certain countries of the European Region. Until general agreement has been reached on how to group the different causes of death, the use of a simple form of tabulation employing the following categories has been proposed:[1] congenital malformations (category A), iso-immunization (B), late fetal death before delivery (C), death during delivery (D), and death during the first week (E).

Time of death

The cause and time of death are closely linked, as brought out by the British Perinatal Mortality Survey made in 1958 (Butler & Bonham, 1963; Butler & Alberman, 1969).

Antepartum fetal mortality. This bears a direct relation to two important complications of pregnancy: toxaemia of pregnancy and antepartum haemorrhage. In the absence of causative treatment, better management of the pregnancy, improved prenatal care, and early diagnosis of pregnancy disorders can help to reduce antepartum fetal mortality.

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[1] Butler, N.R. (1966) *op. cit.*

Intrapartum fetal mortality. The majority of intrapartum deaths occur after more than 37 weeks' gestation and/or in fetuses weighing more than 2500 g (Hirst et al., 1968). Improvements in obstetrical techniques, early identification of fetuses at high risk, and an increase in the number of hospital deliveries (at least for mothers at high risk) can help to reduce this type of mortality.

First-day mortality. Perinatal mortality—particularly early neonatal mortality—is directly related to the number of infants weighing less than 2500 g at birth (Fig. 2). These may be babies born before term with weights corresponding to the stage of fetal development or full-term babies (born between 38 and 42 weeks) with low weights for their gestational age. First-day neonatal mortality is particularly frequent in low-weight infants born before term. Lethal congenital malformations also contribute to this kind of mortality, though to a lesser degree.

Second- to sixth-day mortality. This is associated with low birth weight and consequent lung complications, and with malformations and infections.

Conclusions

Multivariate analysis of the findings of the British Perinatal Mortality Survey of 1958 has singled out the following factors as having a major influence on perinatal mortality:

(1) the social and biological characteristics of the mother;
(2) the obstetrical history;
(3) the course of gestation;
(4) the birth weight of the baby.

The social and biological characteristics of the mother. Those of greatest importance are height, parity, age, and socio-economic circumstances:

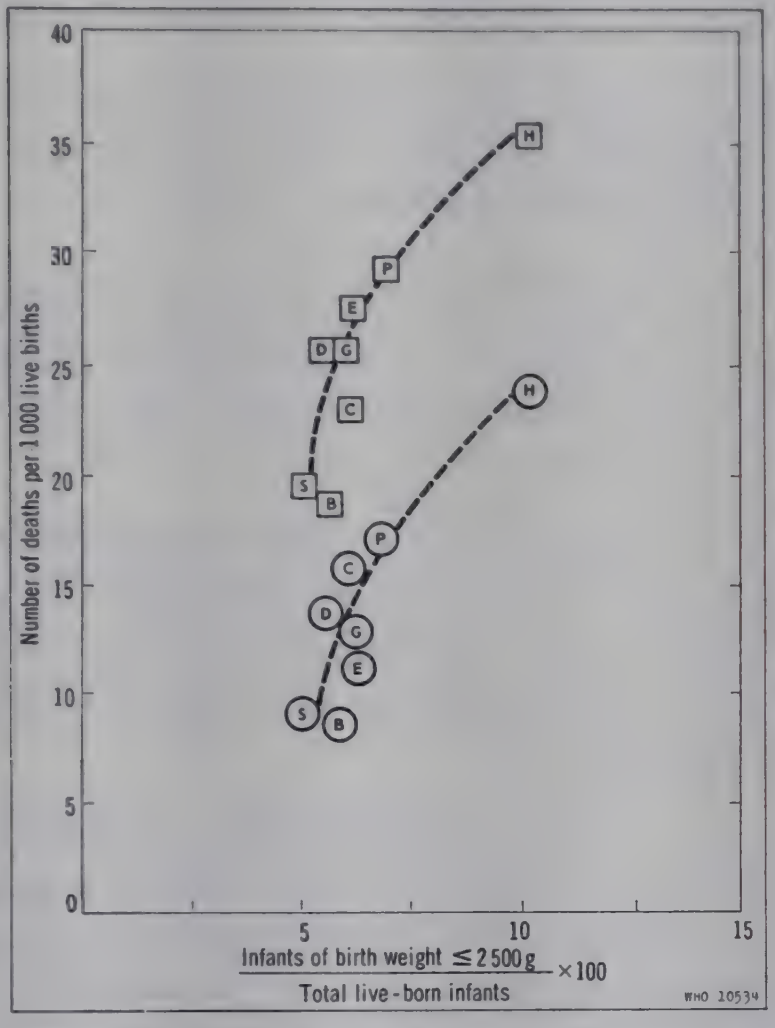
(1) Height (Baird et al., 1953). The risk of perinatal death is much greater for the children of small mothers.

(2) Parity (Butler & Bonham, 1963). At any given age, the risk of perinatal death is lowest for the second and third pregnancies and highest for the fourth and subsequent pregnancies; the risk for the first pregnancy is intermediate between these two levels.

(3) Age. For a given parity, the risk of perinatal death increases rapidly when the mother is over 30. It is well known that the perinatal risk is high when the mother is under 20 years of age, but Feldstein

& Butler (1965) have shown that this increased risk is related to poor social and economic circumstances and to the relatively large number of first pregnancies, rather than to the low age of the mother.

FIG. 2. RELATION OF PERINATAL AND EARLY NEONATAL MORTALITY TO BIRTH WEIGHT IN SEVERAL COUNTRIES OF EUROPE[a]



□ Perinatal mortality
○ Early neonatal mortality
} = f { Low birth weight

[a] B = Bulgaria, 1965; C = Czechoslovakia, 1965; D = Denmark, 1962; E = England & Wales, 1965; G = Democratic Republic of Germany, 1965; H = Hungary, 1965; P = Poland, 1962; S = Sweden, 1966.

(4) Social and economic conditions. The risk of perinatal death is high in the underprivileged classes (Baird et al., 1953; Butler & Bonham, 1963). It decreases as the family's social and economic circumstances improve.

Abnormal obstetrical histories (Febvay & Croze, 1954). A history of previous abortion, perinatal death, the birth of a live child weighing

less than 2500 g, toxaemia of pregnancy, antepartum haemorrhage, or caesarian section indicates an increased risk of perinatal mortality in subsequent pregnancies.

Obstetrical complications. In a study made in England, Scotland and Wales in 1968, perinatal mortality was 8% in the offspring of women suffering from toxaemia of pregnancy (diastolic blood pressure of 100 mm Hg or more, or of 90 mm Hg or more accompanied by proteinuria).

Haemorrhage occurring before the 28th week of gestation was associated with a perinatal mortality of 6%, and massive antepartum haemorrhage with a perinatal mortality of 90%.

Birth weight. The association between perinatal mortality and low birth weight is well known. Perinatal mortality in infants of 2500 g and less is between 30 and 35 times higher than that in infants of over 2500 g. It has been calculated, for example, that a difference of 3% in the number of live-born infants of low birth weight changes the infant mortality rate by 5 per 1000.

From these statistical data it is possible to define the characteristics of the pregnant woman who represents a high risk from the point of view of perinatal mortality. It should be a priority to provide such a woman with special prenatal care and she should be sent, at the appropriate time, to a hospital having the best available facilities for both obstetric and paediatric care.

It should not be assumed, however, that a low perinatal mortality can automatically be equated with a high standard of obstetric and paediatric care and good public health services. Indeed, while the influence of these two factors cannot be denied, there are other variables that should also be examined, such as the definitions and terminology used, the socio-biological and medical characteristics of the population in general and of pregnant women in particular, the frequency of obstetrical complications, and the percentage of infants of low birth weight in relation to the total number of births. Only when all these variables are taken into account is it possible to assess the true significance of perinatal mortality statistics and to make valid comparisons between one country and another.

DEFINITIONS AND NOMENCLATURE

The foregoing considerations demonstrate the urgent need to adopt standard definitions and terminology. Five definitions have already been proposed by WHO: live birth, fetal death, cause of death, under-

lying cause of death, and perinatal period (see Annex 1). In addition, the United Nations Statistical Commission has recommended definitions of length of gestation and birth weight (see Annex 2) which should easily gain acceptance.

Some of these definitions do, however, call for comment. A definition should be based on exact criteria which should be reasonably simple to assess and not liable to subjective interpretation. Thus, the definitions of "live birth" and "fetal death" have proved difficult to apply in practice and allow some latitude of interpretation. It might help if the definitions were simplified by eliminating the criterion "definite movement of voluntary muscles". On the other hand, for the definition of live birth, it might be desirable to fix a minimum length of time (half an hour or possibly an hour) during which the signs of life (breathing and heartbeat) can be observed. This modification becomes all the more urgent as improvements in resuscitation techniques make "life" possible (in cardiovascular terms) in a newborn child that has never breathed on its own nor shown any spontaneous neurological function.

The definition of fetal death should be expanded by introducing the concept of viability so as to establish a lower limit for fetal death and distinguish it clearly from true abortion. Important recommendations on the subdivision of fetal deaths into different groups have been made by WHO (Annex 1), but they are based solely on length of gestation and the uncertain nature of this criterion deprives the recommendations of much of their value.

A similar criticism applies to the definition of the perinatal period, since it is based on the criterion of not less than 28 full weeks of gestation. There are almost insuperable difficulties in using this definition in practice, since the duration of gestation is not or cannot be known in 15–90% of cases, depending on the level of education of the population and the standard of prenatal care.

To be suitable for routine use the definitions should be based solely on the birth weight, which should be required to be shown on both the birth certificate and the death certificate. To distinguish fetal death from abortion, the criterion of viability should also be a minimum weight, e.g., 1000 g or 500 g (the International Federation of Gynecology and Obstetrics has advocated a limit of 750 g). This minimum weight should then also be accepted as the criterion for the registration of a live birth.

Birth weight should be tabulated in steps of 500 g. As in the past, the newborn infant weighing 2500 g or less should continue to be called a "low birth weight infant" and not a "premature infant", a term that should be abandoned once and for all.

The establishment of definitions and terms is not, of course, an end in itself and the purpose for which they are intended should always be kept in view. Similarly, the accuracy of data will vary, depending on whether they are intended for official statistics, epidemiological surveys or operational use in clinical studies. To ensure international comparability of perinatal mortality statistics, it would be useful to lay down minimum criteria—for example, birth weight—to which others could be added as needed and as made possible by improvements in the basic health services. Such additional criteria could include length of gestation or other medico-social parameters of the kind recommended by the fifteenth session of the United Nations Statistical Commission (Annex 2).

CHAPTER 2

SPECIFIC MEDICAL PROBLEMS

MALFORMATIONS

Definition

Congenital anomalies (malformations and inborn errors of metabolism) may be defined as functional or morphological changes in the normal development of the embryo that are present at birth even though they do not always become apparent until later. A distinction should be made between malformations due to the transmission of abnormal genetic information or to a chromosomal aberration, and those due to physical, chemical, or viral factors (e.g., radiation, thalidomide, or rubella) during the critical period of embryonic development. Lastly, certain fetal diseases can give rise to "pseudo-malformations", which should be distinguished from the above (for example, internal hydrocephalus due to postinflammatory stenosis of the aqueduct of Sylvius following toxoplasmic meningoencephalitis).

From the formal genetic standpoint, congenital anomalies may be attributed to 3 types of mechanism:

(1) the action of a single gene (monogenic determination);

(2) secondary effects of chromosomal aberrations;

(3) the simultaneous action of several genes at different loci (polygenic determination).

The distinction between these 3 mechanisms is not only of theoretical interest but also opens up possibilities for preventive measures.

Monogenically determined congenital anomalies. Congenital anomalies due to the action of a single gene constitute only a small group. Some of them may be due to a mutation causing a change in the genetic information. Although this mechanism is rare, it is desirable to make a thorough examination of all the factors known to be capable of increasing the mutation rate.

On the other hand, congenital anomalies due to the substitution of a single gene are only slightly affected, if at all, by environmental influences, so that there can be little hope of preventing them. Nevertheless, for a family with a history of repeated anomalies, the geneticist can supply accurate figures for the risks of recurrences. It is probable that, in the future, amniotic biopsy techniques (followed by culture of the material obtained) will make it possible to provide information on the genotype of the child to be born. Interruption of pregnancy could then be discussed in the light of existing legislation.

Congenital anomalies due to chromosomal aberrations. It is estimated that among every 300 live births, one child carries a major chromosomal aberration, and the incidence is even higher for abortions and stillbirths. Among the factors promoting certain types of chromosomal aberration, the mother's age plays an important part. The incidence of this type of anomaly might be expected to decline considerably if the number of children born to women aged 40 years and over could be reduced. The role of the geneticist is to assess, from appropriate cytogenic examinations, the risk of recurrence in couples who already have one or more affected children.

Polygenically determined congenital anomalies. These anomalies are much more frequent than those described above, as has been found by British research workers investigating such malformations as harelip, with or without cleft palate, congenital dislocation of the hip, pyloric stenosis, and club foot. Studies on twins indicate that malformations of this kind depend on an interaction of environmental factors with the effects of the responsible genes. More extensive family surveys will be needed to enable the risks involved to be worked out exactly and to trace the factor or factors that depend on the environment (particularly the intra-uterine environment). It is probable that new and more thorough family surveys will show that many other congenital malformations belong to this group. It is certain that conventional methods, such as genetic analysis and the study of populations, families and twins, can still provide a great deal of new information regarding the mechanisms underlying congenital malformations.

Frequency

For several years congenital malformations have consistently been responsible for 10–15% of perinatal deaths in males and for 12–28% in females (Butler & Bonham, 1963; Stevenson et al., 1966), with an overall incidence of 3.0 to 8.0 per 1000 live births for girls and 3.2 to

5.8 per 1000 births for boys. This higher death rate among females—especially pronounced for late fetal mortality (Brocke, 1961)—is contrary to what is observed for the vast majority of causes of perinatal death.

The general incidence of congenital malformations detected in the perinatal period, whether in the liveborn infant or in the dead fetus, varies from 1.3% to 2.0% (McKeown & Record, 1960; Stevenson et al., 1966; Butler & Alberman, 1969). Since it is generally admitted that only one out of every two or three malformations is recognized during this period, the overall incidence can be estimated at 3–5%.

There are wide variations between countries in incidence and in types of malformation. A very high incidence of neural tube anomalies (anencephalia, spina bifida, hydrocephalus: 10.55 per 1000 births) has been observed in Northern Ireland (Belfast), where a markedly higher incidence among females explains the higher mortality among that sex. By way of comparison, the incidence of these conditions was 1.5 per 1000 in Yugoslavia and 1.9 per 1000 in Czechoslovakia. It is noteworthy that the risk of anencephalia is higher in urban communities, in families of low socio-economic status, and at the beginning and end of the reproductive period. On the other hand, the incidence of congenital heart disease is three times as high in Spain (Madrid) as in Belfast. Such variations are sometimes real, but may also reflect differences in registration practices. The question can only be settled by fuller epidemiological studies.

Early detection

About 20% of malformations detected at birth are operable. This underlines the value of early diagnosis. Improvements in anaesthetic and surgical techniques and in nursing care during the neonatal period now permit the survival of certain children who formerly would soon have died as a result of their malformation (spina bifida, severe congenital heart disease, oesophageal or duodenal atresia, diaphragmatic hernia). Moreover, certain malformations (dislocation of the hip, malformations of the urinary tract, neuroblastoma) may be cured without sequelae if they are diagnosed and treated at an early stage. This detection must be based first and foremost on a thorough clinical examination, with special attention to the presence of "small" signs (such as the presence of two umbilical vessels instead of three, marked asymmetry of the ears, etc.) and to the case history (hydramnios or oligohydramnios, etc.). This examination should be made during the first hours after birth by a paediatrician; however, the obstetrician, midwife, and paediatric nurse should be aware of the problems involved, so it is necessary to draw up

and give wide distribution to a systematic examination procedure for the detection of congenital malformations in the newborn.

Inborn errors of metabolism

For the most part inborn errors of metabolism are of a recessive nature and their occurrence in any given population may vary considerably. Important progress has recently been made in detecting and treating some of them. Early detection can now be undertaken, as it is now sometimes possible, by an adequate diet begun at an early stage, to prevent the mental deterioration often associated with metabolic disorders of this kind (phenylketonuria, galactosaemia, etc.). Case-finding techniques and all the relevant medical, social and administrative problems have been studied by WHO in recent years (WHO Scientific Group on Haemoglobinopathies and Allied Disorders, 1966; WHO Scientific Group on Screening for Inborn Errors of Metabolism, 1968; WHO Scientific Group on the Standardization of Procedures for the Study of Glucose-6-Phosphate Dehydrogenase, 1967; Wilson & Jungner, 1970).

There is no point in early routine screening unless the basic medico-social services are adequate to permit surveillance, followed by optimum treatment, of the cases thus detected. The institution of routine screening for inborn errors of metabolism should not be considered in isolation, but must be adopted or rejected in the light of the health and economic situation in the country concerned. It is a matter for each government to decide the relevant targets and priorities.

ISO-IMMUNIZATION

This term implies the appearance of antibodies in an organism that has received an antigen originating from a subject of the same species.

Morbidity

During pregnancy, the process of iso-immunization may involve not only erythrocytes, but also thrombocytes and leucocytes. Erythrocytes are by far the most often implicated, giving rise in the fetus and the newborn infant to haemolytic disease of varying severity. Anti-erythrocytic iso-immunization may lead to the intervention of rhesus factors (inducing extremely serious haemolyses), ABO factors or, more rarely, other blood-group factors. In a population where 15% of subjects are rhesus-negative, morbidity of between 0.2% and 0.6% may be expected,

depending on the expressivity of the defect, average parity, and medical practices (frequency of abortions, delivery techniques, frequency of aspecific haemotherapy, etc.). The great majority of Rh iso-immunization cases are connected with anti-D antibodies. Occasionally, other factors (E, e, C, c) are also involved, sometimes with a rhesus-positive (D-positive) mother. Where this situation occurs, the diagnosis is often delayed to the detriment of the newborn infant (kernicterus). Doctors and midwives must be trained to take into account the diagnosis of iso-immunization by other rhesus groups, even if the mother is Rh-positive (D-positive).

Sensitization mechanism

Sensitization occurs following the entry of Rh-positive blood into the maternal circulation, either during delivery (Woodrow & Finn, 1966; Clarke, 1968a) or throughout gestation (Zipursky et al., 1963; Cohen et al., 1964). The degree of sensitization is roughly proportional to the extent of feto-maternal haemorrhage (Clarke, 1968a), but small quantities of blood (e.g., less than 0.2 ml) are enough to induce immunization (*Bull. Wld Hlth Org.*, 1967).

Different pathological conditions may promote the process of iso-immunization: curettage (Hollàn et al., 1967), even in a primipara (J. Rosta—personal communication, 1968); manual detachment of the placenta (Finn et al., 1963); any slightly rough manipulation of the uterus;[1] pre-eclamptic toxaemia (Knox, 1968); amniocentesis (Finn et al., 1963), and perhaps even clamping of the umbilical cord.

Prevention of Rh anti-D iso-immunization

As Table 3 shows, there can be no doubt as to the value of injecting anti-D immunoglobulins (IgG) to prevent iso-immunization:

TABLE 3. EFFECTIVENESS OF THE PREVENTION OF Rh ANTI-D ISO-IMMUNIZATION

	Number of women	Number of patients sensitized
Injection following first pregnancy (Rh+)	1886	4 (0.2%)
Controls	2006	149 (7.2%)
Injections following first and second pregnancies (Rh+)	245	1 (0.4%)
Controls	325	41 (12.6%)

[1] Huntingford, P.J. (1969) *Birth injuries* (Unpublished working document EURO 0410/12).

The injection of 150–200 μg of anti-D immunoglobulins is usually carried out during the first 24 hours (or possibly 48 hours) following delivery. Some authors begin treatment during pregnancy, apparently with no harmful effects on the fetus (Zipursky & Israels, 1967). There are good grounds for applying the same procedure in the case of interruption of pregnancy in any Rh-negative woman. In the event of massive feto-maternal haemorrhage, larger doses of anti-D immunoglobulins may be necessary. The dose should be adjusted according to the persistence or otherwise of fetal blood cells in the maternal circulation, as detected by the acid elution technique of Kleinhauer, Braun & Bekte (1957).

The Medical Research Council of Great Britain is at present conducting therapeutic trials in which four different immunoglobulin dosages (20, 50, 100, and 200 μg) are being used in four groups of women undergoing treatment. When completed, these trials will provide useful guidance as to the best dosage.

The launching of a large-scale prevention programme will depend on the quantity of anti-D IgG available. These immunoglobulins can be obtained (*a*) from persons immunized through pregnancy or transfusion and (*b*) from deliberately immunized volunteers. The theoretical and practical problems involved have been discussed elsewhere (*Bull. Wld Hlth Org.*, 1967).

Where only a limited quantity of anti-D IgG is available, an order of priority should be established in the light of obstetrical, geographical and legal considerations. Theoretically, the acid elution technique could be used to detect fetal globules in the maternal circulation, but this test is delicate and sometimes difficult to interpret, and is not suitable as a general method of detection.

It is recommended that absolute priority be given to all rhesus-negative primiparae giving birth to rhesus-positive children in a compatible ABO group, and then, where anti-D IgG supplies are available, to extend protection to all rhesus-negative primiparae regardless of the child's blood group. Next, protection should be given in later pregnancies, and finally in cases of spontaneous or induced abortion. In a population where 15% of subjects are Rh-negative, the number of primiparae to be treated each year is estimated to vary from 550 to 3300 per million population, depending on the degree of coverage.

Surveillance of pregnancies in Rh-negative women

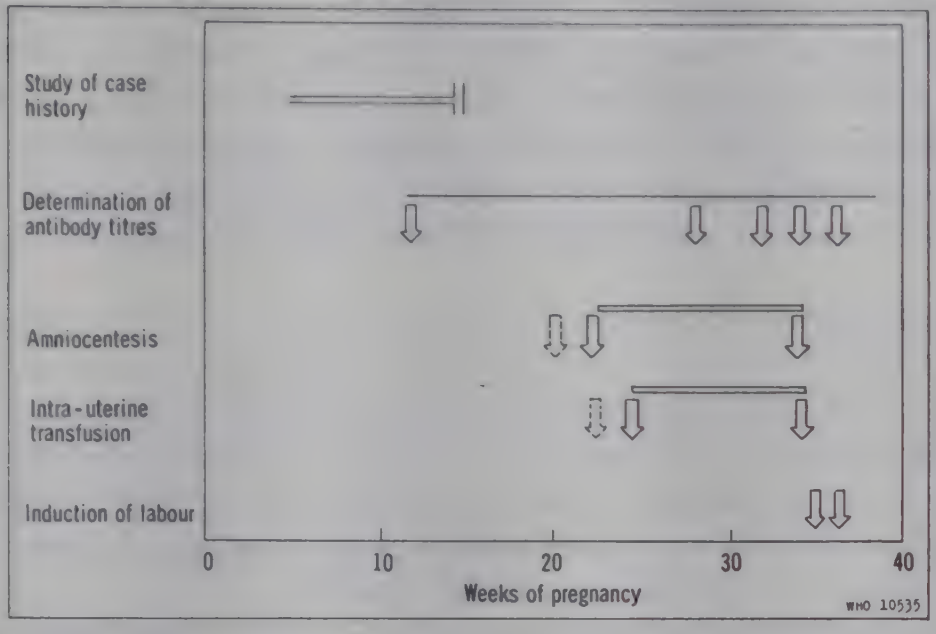
The elements of this surveillance are clearly specified (Fig. 3):

(1) study of case history;

(2) from the 12th week of gestation, examination of the mother's serum for antibodies (to be repeated depending on the features of the case);

(3) in the light of the results of (1) and (2), amniocentesis from the 20th–22nd week and spectrophotometric measurement of the pigmentary content of the amniotic fluid (Liley, 1963).

FIG. 3. TIME-TABLE FOR THE SURVEILLANCE AND INTRA-UTERINE TREATMENT OF Rh-HAEMOLYTIC DISEASE



The findings may bring into consideration an intrauterine transfusion, which is still a hazardous, kill-or-cure procedure, with a mortality rate varying between 60% and 70%. In view of the need for a highly experienced medical team, there is good reason to concentrate all intra-uterine transfusions for a region or a country in a single hospital. Fetal exchange transfusions under hysterotomy have so far given poor results (Freda & Adamsons, 1964).

In cases of acute iso-immunization, the delivery should be induced from the 35th week. To act earlier would mean incurring the drawbacks of immaturity and to wait longer would increase the risk of fetal death.

Extra-uterine treatment

This consists essentially of exchange transfusion decided on and repeated in the light of the indirect bilirubin value. Unjustified surgical procedures should be avoided. Where there is slight iso-immunization it may be advisable to await postnatal developments, provided always that a thorough check is kept on the bilirubin value (Dunn, 1966).

In the case of anasarca or severe anaemia at birth (haemoglobin of 5 g % or less in the blood of the umbilical cord), immediate ventilatory assistance accompanied by precise correction of hypoglycaemia and acidosis and by control of circulatory conditions—it is important to

measure the central venous pressure—will permit the survival of infants that otherwise would not live for exchange transfusion.

OBSTETRICAL AND NEONATAL INFECTIONS

Infections contribute in varying extent to perinatal mortality: 1.5% in Britain (Butler & Bonham, 1963); 1.8% for prenatal infections, and 1.5% for postnatal infections in Czechoslovakia in 1965. Morbidity from infections depends mainly on hospital organization and on the standard of nursing care, but it also has important public health implications owing to the longer stay in hospital often entailed.

Prenatal infections

Except at the end of gestation or at the time of birth, the vast majority of prenatal infections of the fetus are due to a prior infection of the mother. Such prior infections occur all the more frequently where the female population entering the reproductive period has a lower rate of specific antibodies against a particular disease.

The prenatal risk of any given infection in a population can be calculated from a spontaneous infection curve, which will vary from one region to another depending on geographical and epidemiological features (density of population, contacts with zoonoses, and so on).

During the primary infection of the mother, a villous focus is set up from which the embryo or the fetus may become infected. During this placental stage, which takes a certain time to develop, the maternal organism begins to form certain antibodies; this explains the time-lag between infection of the mother and infection of the fetus, known as the prenatal incubation period (Thalhammer, 1967).

Very often a virus infection may induce abortion if it occurs in the embryonic period or may interfere with organogenesis, producing a typical but non-specific embryopathic syndrome. The fetus is relatively protected from the fourth to the sixth month of gestation. At the end of pregnancy, on the other hand, fetal infection more or less characteristic of the virus in question may occur.

Bacterial infections do not seem to give rise to abortions, nor are they thought to cause malformations. In the last three months of gestation they may be responsible for fairly typical fetal infections (for example, listeriosis) and for inducing premature delivery.

Occasionally, protozoan infections (toxoplasmosis) can induce an abortion during the embryonic period. In the fetus the infection may or may not follow a typical course, and the phase of the disease at the

time of delivery will vary widely depending on the duration of the disease in the fetus (recovery complete, with or without sequelae; recovery in progress; disease at its height).

The fetus may react to infection by forming specific IgM antibodies, provided of course that there is a sufficient lapse of time. It was at one time hoped (Stiehm et al., 1966) that the increase in M-immunoglobulins in the blood of the umbilical cord could be used in detecting an antenatal infection. However, this test proved inadequate owing to false negative results (in general, normal IgM in proved cases of infection) and to the possibility of positive (false positive?) results in cases where no known infectious disease could be demonstrated (E. Gautier—personal communication, 1969).

Rubella. Of all the virus diseases, rubella is at present the best known and the most dangerous from the standpoint of teratogenic effects (Australian epidemic, 1940; North American epidemic, 1964). Where clinical rubella occurs in the mother in the first three months of pregnancy, 50–90% of embryos appear to become infected (Dudgeon, 1969), but only some of these will later show malformations (10–67% according to different studies). Further, 15–20% of such pregnancies end in abortion. The same maternal and fetal complications are found in cases of clinically inapparent maternal rubella (Schiff et al., 1965). Maternal infection after the first three months less frequently leads to complications, the incidence of malformations being 0.5–2.2%.

During the North American epidemic, embryonic and fetal lesions consisted not only of fairly typical malformations but also of a generalized syndrome (rubella syndrome or congenital rubella).

Affected newborn infants excrete large quantities of the virus for some months after birth, and this presents practical problems with regard to the protection of staff.

In Europe, 80–87% of women (Rawls et al., 1967), enter the reproductive period with antibodies against rubella. Only women without such antibodies (i.e., 13–20%) are at risk, and they should be vaccinated. Until such time as enough vaccine is available, and more is known about its effectiveness and drawbacks, priority should be given to the vaccination of exposed subjects such as medical and paramedical staff and teachers, possibly after a serological examination.

If a pregnant woman should contract the disease or become exposed to it, gammaglobulin treatment within three days of exposure can be effective (Schiff et al., 1965).

Other virus diseases. These include cytomegalic inclusion disease, measles, chickenpox, poliomyelitis, hepatitis A and B, infectious mono-

nucleosis, mumps, and coxsackievirus and echovirus infections. They may lead to complications similar to those encountered in rubella, although the abortion rate is generally higher. There is a definite risk involved in the use of all live smallpox vaccines during the first three months of pregnancy, and such vaccines should not be used during this period.

Less is known about the effect on the embryo and the fetus of parainfluenzal infections, often reported with the vague designation of "influenza" or "virus disease". However, a study of case histories shows that, after the first three months of pregnancy, such infections are three times as common in women confined before term as in women delivering at full term (Hoyer & Thalhammer, 1968).

Bacterial diseases. Listeriosis, tuberculosis, and *Vibrio fetus* infection (Vincent, 1949) are of some importance, at least in certain countries. Their clinical manifestations vary. It would be useful to carry out blood cultures systematically for all expectant mothers with fever. Similarly, in areas where there is known to be listeriosis, direct bacteriological examination of the meconium for the presence of Gram-positive rods should be undertaken as a routine measure.

The salmonelloses still give rise occasionally to difficulties, mainly problems of diagnosis, because of population movements, especially in western Europe: workers move from south to north, and holiday-makers move from north to south in the summer season. Epidemics in hospital nurseries, originating from infected mothers, still present a serious medical and hygienic problem.

Lastly, cases of endocarditis, peritonitis, osteomyelitis or fetal pyelitis are encountered with varying frequency, and often no pathogenic agent can be identified. Sometimes the case history indicates a bout of fever or a bacterial infection in the mother, or some surgical intervention during pregnancy.

Syphilis. Correct active treatment of maternal syphilis during pregnancy can eliminate the congenital form of this disease. Unfortunately, active congenital syphilis persists because of diagnostic and therapeutic shortcomings. In the newborn child of an infected mother, the serological problem is as follows: the maternal antibodies are G-immunoglobulins, and because of this they enter the fetal circulation, from which they gradually disappear during the weeks following birth. Fetal antibodies of the IgM type can only originate from the fetus itself, and indicate the development of a fetal infection, but production of these antibodies by the fetus is not constant.

Theoretically, therefore, it is possible to distinguish between active

congenital infection and simple serological syphilis through a biological and immunological study of the antibodies in the fetal blood. In practice, however, false negative results make this examination useless.

At present, there are two legitimate approaches to serological congenital syphilis: if the mother has been correctly treated during pregnancy, it will suffice to follow the development of the antibodies, which will disappear within four to eight weeks after birth; if the mother has received no treatment, or inadequate treatment, it is wise to treat the infant as for an active infection.

Toxoplasmosis. In some areas, toxoplasmosis is more frequently encountered than syphilis or other specific conditions. The sources of infection are usually food (pork, rabbit, game, etc.), and close collaboration with the veterinary services is essential in controlling this disease.

If the spontaneous infection curve in a given population shows frequent primary infection in the reproductive period, the routine serological examination of every pregnant woman may be indicated. The treatment of every primary infection in pregnant women should reduce the number of congenital toxoplasmoses: Kräubig & Wolf (1965) reported a reduction from 17% to 5%. At present, there is no irrefutable evidence that toxoplasmosis attacks the fetus in two successive pregnancies (Thalhammer, 1967).

Intrapartum or amniotic infection

Infections occurring just before or during confinement occur more frequently, but less is known about them. In general, they proceed upwards through the vagina, reaching the fetus *via* the amniotic cavity. More rarely, the infection is haematogenic, coming from a placental focus. The causative agents are staphylococci, streptococci, pneumococci, coliform organisms and other Gram-negative pathogens, *Candida albicans*, and herpes virus.

The mother often shows no symptoms. Sometimes, she experiences a bout of fever before, during, or after confinement. The signs of infection (chorionitis, villositis, amnionitis, funiculitis) can be revealed by pathological examination of the placenta or umbilical cord.

Only some 30% of children born under known conditions of amniotic infection, as demonstrated by histological examination of the placenta, show patent infection, either localized in the respiratory system (otitis, pneumopathy) or alimentary tract, or of a general nature (meningitis, septicaemia) (Anderson et al., 1962; Pryles et al., 1963).

The following situations may be associated with infection of the newborn infant:

(1) various obstetrical procedures, including amnioscopy;
(2) rupture of the amniotic sac 24 hours or more before delivery;
(3) unexplained fetal tachycardia;
(4) temperature exceeding 37.5°C in the mother during labour;
(5) labour continuing for more than 24 hours;
(6) funiculitis on histological examination of the umbilical cord (may also be encountered during chronic or subacute fetal hypoxia);
(7) leucocytes or micro-organisms in the gastric juice.

Preventive treatment of the newborn infant, where the case history or examination shows one of these potentially dangerous conditions, has not yet proved successful. Moreover, massive administration of antibiotics might encourage the multiplication of Gram-negative agents of low pathogenicity, thus rendering them more virulent. The best form of prevention is the induction and rapid termination of labour, provided that pregnancy has lasted at least 34 weeks. The newborn infant will then be at high perinatal risk and should be placed under strict observation in a special care unit. Any behavioural anomaly or the manifestation of unexplained "small" symptoms should be followed up by a series of bacteriological investigations (lumbar puncture, blood culture, urine culture, etc.). If a diagnosis of neonatal infection then becomes likely or certain, vigorous and appropriate antibiotic treatment should be initiated, avoiding as far as possible the use of drugs that are dangerous at this age, such as chloramphenicol, tetracycline, and the sulfonamides.

In the case of recurrent maternal genital herpes, there may be grounds for considering delivery by caesarean section.

Postnatal infection

Colonization of the newborn infant. At birth, the child comes from a sterile environment into an extra-uterine environment teeming with saprophytes and infectious agents (bacteria, viruses, and moulds). It is very rapidly colonized in successive stages: naso-oro-pharyngeal cavity, then the umbilical region, and finally the skin surface (with marked differences between the sexes.) Usually this colonization is conducted by a variety of germs which, in time, strike a mutual balance. External colonization appears to be completed within 8–12 hours of birth, but in the alimentary tract colonization continues in a manner varying with the infant's diet.

The newborn infant is partially protected by IgG-type antibodies passed on to him from the maternal circulation from the 28th–30th week of gestation. The IgG level in the newborn infant is equal to or

slightly higher than that of the mother at full term. If delivery takes place before term, the IgG level in the infant is lower. Moreover, the normal absence of IgM deprives the newborn infant of antibodies against Gram-negative organisms. Added to this, the phagocytic properties of the leucocytes do not appear to be as great in the infant as in the adult. Thus, in the course of the first day of extra-uterine life, a fairly unstable balance is established between the micro-organisms colonizing the newborn child and his inadequate and unpractised defence mechanisms. This balance depends on the quantity of pathogenic organisms, on whether one or several types of organisms are present, on the degree of pathogenicity, on the quality of the infant's epidermis and mucous membranes (umbilical and skin lesions, etc.), and on the length of gestation.

Other factors, such as the phagocytic activity of the leucocytes, also enter into consideration, but there is still insufficient information about their role.

Normal colonization is desirable, and in any case difficult to avoid. Nevertheless, massive colonization by a single agent (for example, staphylococci, *Pseudomonas aeruginosa*, etc.) must be prevented.

Hospital infections. The differences between normal colonization of the newborn infant, the development of a postnatal infection, the septicaemic generalization of such an infection in the child concerned, and finally its spread to a whole nursery, are purely quantitative. Indeed, during a hospital infection, the pathogens disseminated are usually of low virulence and often resistant to antibiotics, following the same principles as those governing the colonization of the newborn infant.

Hospital infection is spread by contact (hands, utensils, linen, food) and by air. Owing to the vulnerability of the newborn infant, therefore, a particular watch must be kept on these routes of transmission and efforts made to block them (see Annex 3).

BIRTH WEIGHT AND FETAL GROWTH

Length of gestation

The purpose of all gestation, as of all prenatal care, is to bring the fetus to a state of maturity that will enable it to withstand without harm the normal and necessary stresses of labour and to adapt rapidly to extra-uterine life: to breathe, to take the breast, to carry out the processes of digestion and metabolism, to eliminate bilirubin in sufficient quantity, and to regulate its temperature—in short, to live and grow without further assistance under normal conditions (Kloosterman, 1968).

This state of maturity is usually achieved after a gestation period of 280 days, counting from the first day of the last period, with a physiological deviation ranging from the beginning of the 38th week (259 days) to the end of the 41st week (293 days).

Any shortening or prolongation of gestation is marked by an increase in perinatal mortality, particularly pronounced in the case of shorter gestation and fairly closely proportional to the size of the deviation from the normal duration (see Table 4).

TABLE 4. RELATION BETWEEN PERINATAL MORTALITY AND LENGTH OF GESTATION (CZECHOSLOVAKIA, 1967)

Length of gestation (days)	No. of deliveries (approx.)	Perinatal mortality (%)
258 or less	12 500	25.2
259-293	194 000	0.7
294 or over	10 900	1.7

Birth before term (258 days or less) is associated with perinatal mortality 33 times higher than for normal delivery, while the perinatal mortality for prolonged pregnancies (294 days and over) is double the figure for delivery at full term.

Somatic growth

With certain reservations, somatic growth may be regarded as a useful criterion of general fetal growth. As a rule, fetal weight doubles every 6 weeks from the 28th week of gestation. However, after the 38th week there is a certain slowing down following diminished placental support (Gruenwald, 1966). Several factors that can still be regarded as normal may affect the intra-uterine increase in weight. (The distinction between "normal" and "pathological" factors is arbitrary and unscientific, but useful from a practical standpoint.)

(*a*) *Factors associated with the genetic characters of the fertilized ovum*

From the 20th week of gestation, the male fetus increases in weight more rapidly than the female fetus, with differences of 50 g at 32 weeks and 150 g at 40 and 44 weeks. On the other hand, the weight of the placenta is identical in both sexes, so that the male fetus makes greater demands on the placenta than does the female fetus.

(*b*) *Biological characters of the mother (and the uterus)*

Stature (Butler & Alberman, 1969). Where all other conditions are equal, birth weight varies with the height of the mother, a tall mother having a child with a higher birth weight and a short mother a child with a lower birth weight; thus, at 40 weeks, there is a difference in birth weight of 250 g between the child of a mother of 164 cm or more and that of a mother of 158 cm or less.

Parity (Kloosterman, 1968). The birth weight of children of primiparae is significantly lower than that of children of multiparae from the 32nd week of gestation; there is a difference of 120 g at 36 weeks, 200 g at 40 weeks, and 180 g at 44 weeks.

Twinning (McKeown & Record, 1952). Weight gain slows down after the 31st week, when the two fetuses reach a combined weight of 3000 g. The gain slows even earlier in the case of multiple pregnancies.

Birth weight of mother (Ounsted, 1968). The mother's birth weight and that of the child appear to correspond.

Mode of contact between ovum and mother (Kloosterman, 1968). Umbilical cord insertion anomalies are associated with delayed weight gain. There is a difference of 340 g between velar and paracental insertion at 40 weeks' gestation.

(*c*) *Extrinsic factors (due to maternal environment)*

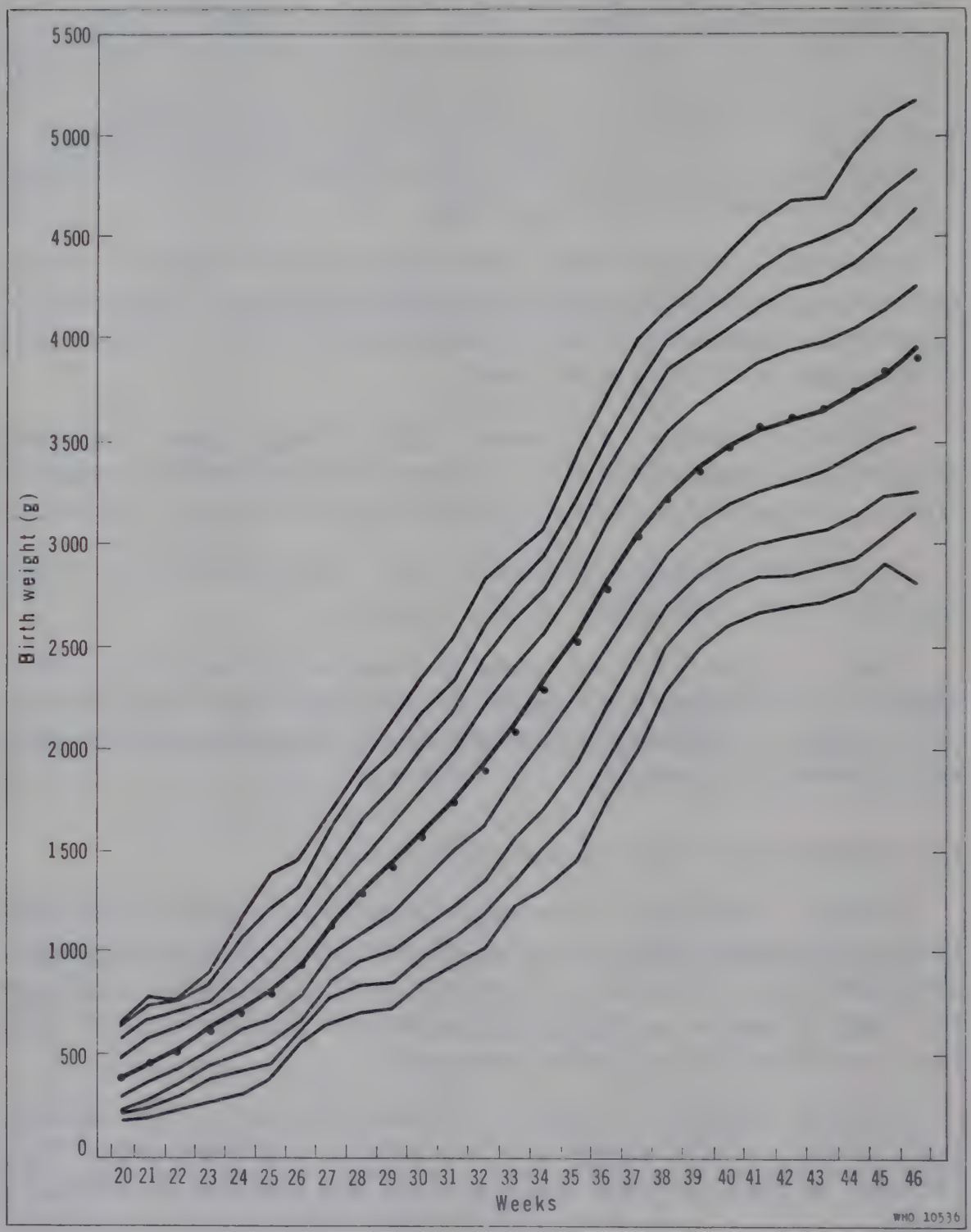
Feeding. An extreme reduction in the expectant mother's food intake (Leningrad siege of 1942; famine in the west of the Netherlands, winter 1944-1945) may reduce the fetal weight gain. The dietary conditions to which the mother is exposed throughout her growth are even more important than feeding during pregnancy.

Cigarette smoking. It has been definitely established that cigarette smoking reduces fetal weight gain, the reduction in birth weight being in direct proportion to the amount of smoking (Butler & Alberman, 1969).

High altitude. Mothers living at altitudes above 3000 m give birth to infants of lower than normal weight (Lubchenko et al., 1968).

The more general factors controlling fetal weight gain are not yet fully known. Besides the quality and quantity of the nutrient flow across the placental barrier, it would be appropriate to consider the possible role of a maternal regulator or even of antigenic disparity between the fetus and the mother (Ounsted, 1968).

FIG. 4. BIRTH WEIGHT AND LENGTH OF PREGNANCY[a]



[a] Data collected during a study of 80 000 cases in a school of midwifery (1948-1957) and in a university clinic in Amsterdam (1931-1965).

From the practical standpoint, any evaluation of birth weight in terms of length of gestation implies the use of a reference curve showing weight gain. Several reference curves are at present available for European countries: Britain (Butler & Alberman, 1969), Sweden (Lindell,

1956), the Netherlands (Kloosterman, 1968, see Fig. 4), and Hungary (J. Rosta—personal communication, 1969). It would be useful to prepare others to meet the needs of the various regions before combining them all in a single curve. The same applies to the preparation of reference curves for length and cranial circumference.

Visceral development

In evaluating fetal growth, there are other important aspects besides weight, length, and cranial circumference, but they are difficult to express in terms of figures.

During the second half of gestation the liver of the fetus undergoes marked enzymatic changes, leading finally to the constitution of large reserves of glycogens. These reserves will be rapidly used by the infant in the hours immediately following delivery (WHO Scientific Group on the Effects of Labour on the Foetus and the Newborn, 1965).

The establishment of glycogen reserves at myocardial level is also of the utmost importance in enabling the fetus to maintain sufficient cardiovascular activity during delivery, when transplacental gaseous exchange may be temporarily inadequate.

Towards the 22nd week of gestation, major biochemical changes take place in the primitive bronchial epithelium, permitting the formation of tensio-active (surfactant) phospholipids that are readily mobilized; when the alveoli have been aerated, these phospholipids enable them to be stabilized during the respiratory cycle.

The central nervous system undergoes important quantitative and qualitative changes throughout the fetal period. The number of neurons increases, reaching a maximum towards the 36th week of gestation (Rabinowicz, 1967), the enzymes mature (differing from region to region), synapses are established, myelinization begins, and the capillary network develops. These various processes are still far from completed at birth. An important feature of the brain of a baby at birth is that its cellular density is greater, weight for weight, than that of the adult brain; however, it has a poorer capillary network, and this certainly contributes to circulatory vulnerability.

This differentiation of the central nervous system is expressed in neurological development week by week. Indeed, neurological maturation is strictly proportional to the chronological age of the fetus, regardless of weight gain (Thomas & Saint-Anne Dargassies, 1952). This makes it possible to assess the length of gestation without reference to the case history or to weight gain. Similarly, the EEG (Dreyfus-Brisac et al., 1962) and the electromyogram show changes strictly corresponding to fetal age.

Moreover, the appearance of the fetal membranes varies with the length of pregnancy, which makes it possible to make an estimate of gestational age (Usher et al., 1966).

It is not easy to assess the maturity of the newborn infant. Up to a point, postconceptional age can be estimated on the basis of outward appearance, clinical examination, and assessment of neurological development (neurological examination, EEG, EMG). Nevertheless, it is not yet possible to determine the degree of maturity of the newborn infant from its length and weight and in relation to postconceptional age.

Weight anomalies

Despite what has been said, birth weight remains an important parameter in assessing the health of every newborn infant. In relation to postconceptional age, deviations in either direction are possible.

Accelerated weight gain. Weights above percentile 97 are considered pathological, no matter what the length of gestation. An accelerated weight gain occurs in the children of diabetic or prediabetic mothers and also in some children born well before term, regardless of any error in assessing the length of gestation. Perinatal morbidity in these infants corresponds to the length of gestation, not to birth weight (Battaglia et al., 1966).

The child of a diabetic or prediabetic mother presents several perinatal problems: malformations occur more frequently; there is almost always early postnatal hypoglycaemia, linked with the hyperinsulinism induced by the maternal disease; there may be respiratory and metabolic disorders, clearly related to the length of gestation and not to weight.

More than anything else, the child of the diabetic mother is exposed to obstetrical manipulations (artificial inducement of labour, breech extraction, caesarian section) that increase the risk of birth injuries and hypoxia, especially as its excessive weight and length often make the fetus too large for the pelvis.

In certain cases, the increase in rate of growth exceeds placental capacity; this leads to metabolic insufficiency accompanied by subacute fetal hypoxia, which is often responsible for severe neonatal asphyxia and subsequent respiratory disorders.

Retarded weight gain. A distinction should be made between the low-birth-weight infant, a term reserved for those weighing 2500 g or less regardless of the length of gestation (i.e., a purely epidemiological designation for statistical purposes), and newborn infants that are "small for date" and whose birth weight is under percentile 3 in relation

to the length of gestation. Such a child may be born before term, at full term, or after term. There are a number of reasons for this retarded fetal weight gain. It should be recalled that certain conditions—including some that are regarded as normal, such as primiparity, multiple pregnancies, excessive cigarette smoking, highly inadequate food intake, and life at a high altitude—are associated with low birth weights, but rarely with weights below percentile 3. The pathological conditions responsible for delaying intra-uterine weight gain are connected with the fetus, with the mother, and particularly with the state of the placenta.

Pathological conditions connected with the fetus include:

(1) malformations, chiefly malformations of the alimentary tract or cardiovascular system (excluding transposition of the large vessels);
(2) osteogenesis imperfecta;
(3) chromosomal aberrations: trisomies 21, 16-18, 13-15, Turner's syndrome, deletion of short arm of C5;
(4) multiple malformation syndromes: Silver's syndrome, Cornelia de Lange's syndrome, Seckel's syndrome;
(5) intra-uterine infections: congenital rubella, cytomegalic inclusion disease, congenital syphilis, toxoplasmosis;
(6) severe intoxications: cytostatic treatment, extensive exposure to radiation.

Pathological conditions connected with the placenta and the mother include:

(1) uterine vascularization anomalies (pre-eclamptic toxaemia, maternal hypertension);
(2) placental insufficiency.

Of all the conditions responsible for retarded weight gain, placental insufficiency is the most frequent. The appearance of the fetus is highly characteristic, so much so that the term "dysmature" is reserved for newborn infants that have suffered from placental insufficiency *in utero*.

Births before or after term

1. *Infants born before term (formerly known as premature or pre-term infants)*

It is usual to consider any baby born before the 259th day of pregnancy as born prematurely or before term. The words premature and prematurity lead to confusion, since they are still too often linked with the idea of low birth weight (2500 g or less). It would be better to drop these terms, or at least to use them solely for babies born before the 259th day of pregnancy.

The mechanisms by which labour is initiated before term can only be explained when the factors determining the induction of full-term delivery (pituitary-adrenal axis, respective roles of placenta and of fetus) are known. Meanwhile, all that can be done is to relate pre-term delivery to certain well-defined pathological conditions, which is possible in 50% of cases.

Pathological conditions that may be present in the mother before conception are:

(1) Congenital uterine malformations.

(2) Dilatation of the cervix uteri. The cause of this anomaly, which leads to repeated deliveries before term, is not well understood: an association with previous abortions is increasingly being revealed. Table 5 shows a striking correlation between the incidence of legal abortions carried out under good technical conditions and the number of deliveries before term. It therefore seems that interruption of pregnancy, although it eliminates fetuses at high risk (see page 16), causes morphological and functional changes in the uterus that eventually promote deliveries before term. Similar observations have been reported from Hungary, Romania, and the USSR.

TABLE 5. ASSOCIATION BETWEEN ABORTIONS AND PRE-TERM DELIVERIES

	Czechoslovakia	Prague
Number of births	217 421	10 829
Number of abortions	96 421	9 009
Ratio of legal abortions to births	0.44	0.83
Pre-term deliveries (%)	5.8	8.9
Perinatal mortality (per 1000)	21.6	25.1

[a] Afeter Štembera, Z. K. (personal communication, 1969).

(3) Maternal cardiac volume: pregnancy is accompanied by important cardiovascular changes in the mother. In particular, cardiac output increases sharply if the myocardial functional reserve is sufficient. Radiological measurement of maternal cardiac volume can give an idea of the size of the myocardial functional reserve. Certain authors (Raiha, 1964) believe there is a close relationship between insufficient cardiac volume and the probability of pre-term delivery, and that such delivery can sometimes be avoided by ordering rest for pregnant women with a low cardiac volume (who are often of small build as well).

Pathological conditions appearing during pregnancy are:

(1) Antenatal haemorrhage (with or without placenta praevia) with threatened miscarriage, and pre-eclamptic toxaemia. Little is yet known of the physiopathology of these two conditions, which are responsible for many deliveries before term, with a particularly high perinatal mortality.

(2) Acute maternal infection. Some maternal infections, such as listeriosis, are responsible not only for fetal infections, but also for inducing labour before term, whatever the length of gestation.

(3) Maternal bacteriuria. Some authors (Kass, 1960) have drawn attention to the association between bacteriuria (whether symptomatic or not) in the mother and the inducement of labour before term. These observations are still awaiting confirmation.

The above pathological conditions often lead to delivery before term. It might be useful, for preventive purposes, to calculate this risk, and this has been attempted by Papiernik-Berkhauer (1969).

In 50% of pre-term deliveries it is not possible to establish any definite pathological cause, but unfavourable socio-biological features are often found in the mother (high parity, pregnancy early or late in reproductive period, small stature, etc.). Special prenatal care for pregnant women in these high-risk groups would reduce the number of pre-term deliveries, and this in turn would significantly reduce perinatal morbidity and mortality.

The postnatal prognosis in the event of a delivery before term depends on the gestational age—the limit of viability lies between 25 and 26 weeks—and on the presence or otherwise of pathological pregnancy situations that may have compromised the intra-uterine development of the fetus.

The less advanced the postconceptional development of the newborn, the higher the neonatal morbidity. It is rare not to find some complication in a child born after gestation of 32 weeks or less.

In most cases, complications can be predicted from the case history and from the results of the initial clinical examination made at or shortly after birth. Proper medical and nursing care from the time of birth (correct ambient temperature, optimum oxygenation, correction of metabolic changes) can prevent these complications from setting in or at least mitigate their severity.

Complications related to birth before term are:

(1) Hyaline membrane disease, which is frequent and serious at 33 weeks' gestation or less, less frequent and more amenable to treatment from the 34th week, and rare after the 38th week.

(2) Recurring apnoea, which appears after the first 24 hours and has no relation to a pulmonary attack.

(3) Metabolic disorders, such as hypoglycaemia and hypocalcaemia.

(4) Hyperbilirubinaemia, which occurs before the fifth postnatal day and progresses slowly. The danger of kernicterus increases in the event of metabolic or respiratory acidosis or of hypoglycaemia following the administration of certain drugs to the mother or the newborn (sulfonamides, hydrosoluble vitamin K, salicylates).

(5) Tendency towards late metabolic acidosis.

(6) Increased susceptibility to infection.

(7) Haemorrhagiparous syndrome.

2. *Children born after term (formerly known as postmature or post-term infants)*

Statistics indicate that the prevalence of deliveries after term, i.e., at 294 days or later, varies considerably: 5% in Czechoslovakia (Štembera),[1] 12% in the United Kingdom (Butler & Alberman, 1969). Not every birth after term is necessarily pathological, but there is a certain increase in perinatal mortality and this is particularly marked in primiparae giving birth to male infants (Kloosterman, 1968).

These infants are sometimes called postmature, but the term implies not only a delay in delivery, but also a greater degree of maturity than that for 280 days' gestation. It would therefore be better to drop the expression.

Little is known of the reasons why pregnancy is prolonged, but the resulting risks are familiar:

(1) Risk of intra-uterine hypoxia: the gap between the needs of the fetus and the capacity of the placenta to meet them, particularly where gaseous exchange is concerned, becomes greater and greater; eventually the placenta is inadequate, and in as many as 40% of prolonged pregnancies the fetus shows signs of intra-uterine hypoxia (Table 6).

(2) Higher risk of birth injury. The fetus, and particularly the skull, continues to develop, and reaches such dimensions that feto-pelvic disproportion becomes more frequent. Ossification of the cranium is also more advanced and this reduces its adaptability to the pelvic aperture.

Any prolonged pregnancy is potentially a high-risk pregnancy and should be carefully followed (repeated amnioscopy) to permit the early detection of signs of placental insufficiency. The appearance of such signs will indicate when gestation should be brought to an end (by caesarian section or inducement of labour by the vaginal route).

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[1] Štembera, Z.K. (1969) *Prematurity and postmaturity (premature labour and prolonged gestation).* Unpublished working document EURO 0410/9.

TABLE 6. FREQUENCY OF SIGNS OF INTRA-UTERINE HYPOXIA IN RELATION TO LENGTH OF GESTATION[a]

Signs of hypoxia	Length of gestation	
	38-42 weeks	> 42 weeks
Meconial coloration in amniotic fluid	8%	19%
Bradycardia	3%	7%
Meconial coloration plus bradycardia	3%	14%
Total	14%	40%

[a] After Štembera, Z. K. (personal communication, 1969).

The newborn infant may present the following complications:

(1) Cerebral disorders due to intrapartum hypoxia or perinatal asphyxia.

(2) Metabolic disorders, principally hypoglycaemia.

(3) Birth injury.

(4) Asphyxia at birth, possibly followed by respiratory complications.

Disparity between weight and maturity: the dysmature newborn

The fetus, a true parasite, depends entirely for its growth and maturation on the metabolic qualities (nutritive functions) of the placenta and on effective gaseous exchange (respiratory factors) through the intra-placental circulation. In the absence of biochemical or physiological tests for assessing the quantity and quality of exchanges between mother and fetus, a diagnosis of placental insufficiency can be made *retrospectively*, after birth, on the basis of the characteristic appearance of the baby (reflecting intra-uterine malnutrition) and its behaviour during the neonatal period. This type of infant is called dysmature. The term should be applied only to babies that have suffered from placental insufficiency *in utero*.

Dysmaturity may be preceded by gross placental lesions (fairly large infarcts) or by microscopic lesions (Gruenwald, 1964). In most cases, however, no placental lesion can be demonstrated. Clinically speaking, placental insufficiency is often associated with pre-eclamptic toxaemia, with utero-placental circulation anomalies, and with vascular accidents in the mother.

Means of diagnosis prior to delivery are limited: inadequate weight gain by the mother, insufficient increase in uterine volume (abdominal circumference, position of the fundus), oligohydramnios. The 24-hour oestriol excretion, ultrasonic measurement of the growth of the head of the fetus, and amnioscopy can confirm the clinical impression.

Placental insufficiency may set in at any time during pregnancy. The dysmature infant may be born before term, at full term, or after term. If born before term, it will present the typical neonatal complications of dysmaturity and prematurity.

Moreover, dysmature infants can be divided into three subgroups (Table 7), depending on the duration of placental insufficiency, when and how quickly it sets in, and the preponderance of nutritive or respiratory insufficiency.

TABLE 7. DIFFERENT TYPES OF DYSMATURITY

	Placental insufficiency		
	Acute	Subacute	Chronic
Mechanism	Impairment of respiratory function predominant	Impairment of nutritive function predominant	
Rate of outset	Rapid	Fairly slow	Slow
Intensity	Variable	Medium	Severe
Weight gain Growth in stature Cerebral growth	Slightly retarded Normal Normal	Slightly/considerably retarded Normal Normal	Considerably retarded Considerably retarded Slightly retarded
Appearance of newborn	Thin; desquamation of skin; meconial staining	Thin, long with large head	Small, short, with relatively large head
Neonatal complications	Asphyxia; respiratory distress, postasphyxial syndrome with inhalation of amniotic (meconial) fluid	Hypoglycaemia (the higher the head: birth weight ratio, the more serious the hypoglycaemia) Hypothermia	

Acute placental insufficiency is generally seen in infants born at full term or after a prolonged pregnancy. They are somewhat underweight, but length and cranial circumference are normal. The external appearance is typical, with desquamation of the skin on the palms and soles and meconial staining (Clifford, 1954).

Subacute placental insufficiency is found in children born at full term or before term: weight gain is retarded, but growth in stature and cerebral development are normal. Occasionally cutaneous desquamation and meconial staining can be observed.

Chronic placental insufficiency may be encountered at any period of gestation. There is a very marked retardation of growth, both in weight and stature, and also a relatively slight diminution of cerebral development.

Finally, any association of the different forms of placental insufficiency may be seen.

Placental insufficiency affects the fetus in a number of different ways:

(1) Impairment, first of weight gain, then of increase in length, and finally of cerebral development.

(2) Appearance of signs of fetal distress due to intra-uterine hypoxia: elimination of meconium and meconial coloration of the amniotic fluid, meconial staining of the cord and of the fetal membranes.

(3) Poor resistance of the cardiovascular system in the event of asphyxia, e.g., at the moment of delivery (owing to metabolic disorders of the myocardium).

(4) Onset of fairly severe postnatal hypoglycaemia during the first 24 hours, with or without clinical manifestations (absence of liver glycogen).

(5) Postnatal decline in weight insignificant or nil.

(6) Frequency of some degree of dehydration.

(7) More rarely, appearance of respiratory distress associated with massive alveolar haemorrhage.

(8) Possible neurological disorders of varying intensity, difficult to interpret: postanoxic encephalopathy, role of hypoglycaemia, effect of malnutrition on cerebral development.

Conclusions

The detailed consideration of birth weight in the light of information from the case history, counter-checked against data from the clinical examination (somatic and neurological), associated where necessary with paraclinical examinations (radiography, EEG, EMG), makes it possible to assess fetal growth and, up to a certain point, maturity. If the birth weight is above the 97th percentile or below the 3rd percentile

in relation to gestational age, or if delivery occurs before 259 days or later than 293 days of gestation, this should be regarded as pathological and the newborn infant should be placed in the high-risk group. The complications specific to these different situations can be foreseen, avoided to a greater or lesser extent, and in any case often mitigated by adequate medical and nursing care.

Exact classification of the newborn child at birth, moreover, will facilitate any later retrospective evaluation and make it possible for any developmental anomalies that may occur later to be linked more accurately with a specific pathological situation in the perinatal period. Indeed, some current catamnestic studies are difficult to interpret owing to the absence of reliable clinical and biological information from the perinatal period. In this connexion, it would be useful to standardize the nomenclature for the different types of newborn infant (see Annex 1).

PERINATAL HYPOXIA

This term denotes a pathological situation characterized by lack of oxygen in the tissues. Hypoxia is the most common cause of late fetal mortality (antepartum and intrapartum) and of early neonatal mortality. Furthermore, non-lethal but prolonged hypoxic conditions in the perinatal period may be responsible for cerebral lesions that will subsequently manifest themselves in psychomotor developmental disorders or in mental deficiency.

Placental gaseous exchange

Experiments with animals have made it possible to establish how transplacental gases are transferred (Dawes, 1968), but the exact relation between the maternal and fetal circulations in the human placenta is still a matter for hypothesis. On either side of the placental barrier, the crucial parameter is the oxygen transport capacity, i.e., the blood flow multiplied by the oxygen content of the blood. To calculate this, a number of factors have to be known: the blood flow, the haemoglobin rate, the haemoglobin affinity for oxygen, and the partial pressure of the oxygen.

On the mother's side, a preliminary estimate gives an oxygen transport capacity of about 40 ml per minute, matched on the fetal side by a capacity of 36 ml per minute. The oxygen consumption of a fetus at full term is about 15 ml per minute, so that under normal conditions, in the absence of utero-placental circulation anomalies or of any disturbance of the placental barrier proper, there is a certain safety margin

between supply and demand. This calculation shows the importance of two factors, haemoglobin rate and oxygen saturation, in both the mother and the child. On the mother's side, anaemia of 8 g or less haemoglobin per 100 ml or a haemoglobin saturation rate of 70% or less dangerously reduces the oxygen transport capacity and, as a result, the fetal oxygen intake. The outside limits are 5 g haemoglobin per 100 ml and 50% saturation.

At the end of pregnancy, under normal conditions, there is no indication that the oxygen supply to the human fetus is insufficient. At the onset of labour, the partial oxygen pressure of the arterialized blood of the fetal scalp is between 20 and 25 mm Hg, corresponding to a saturation rate of at least 50%. The pH is normal, showing no deviation either in the metabolic component or in the partial CO_2 pressure.

During normal labour respiratory acidosis with hypoxaemia of feto-placental origin sets in, associated with metabolic acidosis of maternal or placental origin. The mixed acidosis found in the blood of the umbilical cord originates therefore during the actual parturition.

The situation in the case of fetal asphyxia is quite different. This appears in the blood, through an exacerbation of the respiratory acidosis and hypoxaemia, and through the onset of hypoxaemic lactic acidosis of fetal origin, with a marked excess of lactate reflecting hypoxia of the tissues.

Antenatal and intrapartum fetal hypoxia

Four causes of hypoxia are distinguished, depending on the point at which the oxygen supply system is disturbed between its intake by the placenta and its use by the fetal tissue:

(1) Anoxic hypoxia due to insufficient oxygenation of the fetal blood in the placenta: inadequate oxygen supply from the mother, inadequate maternal cardiac output, maternal anaemia (8 g or less haemoglobin per 100 ml), utero-placental vascularization anomalies, reduction of the placental exchange surface (normal area: 11.0 ± 1.5 m^2), thickening of the placental barrier.

(2) Anaemic hypoxia: insufficient oxygen circulating in the blood of the fetus as a result of severe anaemia: by feto-maternal transfusion or, in the case of twins, interfetal transfusion; haemolytic anaemia during iso-immunization.

(3) Hypoxia by stasis: reduction in blood flow caused either by fetal cardiac insufficiency (plethora due to materno-fetal transfusion or, in the case of twins, interfetal transfusion) or by insufficient circulation, whether general or regional (accidents of the umbilical cord).

(4) Histotoxic hypoxia: inadequate utilization of oxygen in the fetal tissue: cellular intoxication (e.g., by barbiturates).

Indeed, practically all pathological obstetrical situations ultimately interfere with the oxygen supply to the fetus, and local or general anaesthesia may exacerbate this situation still further.

Detection and treatment of fetal hypoxia

For a very long time, the obstetrician and the midwife had to rely on clinical signs for the diagnosis of fetal hypoxia: change in heart rate, meconium emission (presence of meconium in the amniotic fluid on rupture of the membranes), decline in fetal motor activity. New methods have now been added to the means of diagnosis: thanks to amnioscopy, meconium emission into the amniotic fluid can be demonstrated before rupture of the membranes; moreover, continuous recording of the fetal heart beat, in association with recording of the uterine contractions during labour (tococardiography), makes it possible to measure cardiac activity over long periods and to assess the effect of the contractions on the fetal heart rate. It is thus possible to distinguish between different types of cardiac depression of varying clinical significance (WHO Scientific Group on the Effects of Labour on the Foetus and the Newborn, 1965).

During delivery, once the amniotic sac has broken, it is possible to follow the acid-base parameters of the fetal blood; changes in the direction of acidosis indicate significant disorders in the fetus.

These different methods help in understanding what may be taking place *in utero*, particularly during delivery. They have become indispensable for the early detection of fetal hypoxia, and are so effective that every obstetrics department should be able to make use of them. The introduction of these techniques for continuous observation of the fetus provides a better foundation on which to base treatment decisions; for example, the decision whether to let a breech delivery continue or to intervene swiftly and perform a caesarian section.

The effect of oxygenation of the mother during labour has long been a matter of controversy. In fact, it can be beneficial for the fetus (moderate rise in fetal pO_2), but care must be taken to avoid maternal hypocapnia since reduction of the maternal pCO_2 by hyperventilation, however induced, will reduce the partial oxygen pressure in the fetus and thus place it at risk of hypoxia.

Establishment of breathing

A certain number of conditions have to be met to enable breathing to be established:

(1) The respiratory centres must respond to external and internal stimuli.

(2) The lungs must be sufficiently mature: alveolo-capillary barriers formed, presence of surface-active phospholipids that can be mobilized and rapidly renewed.

(3) There must be no major malformations of the respiratory tract.

Once the baby is free of the mother's body, different mechanisms for cardiorespiratory adaptation come into operation:

(1) Disinhibition of the respiratory centres by external stimuli or owing to hypoxia and acidosis.

(2) Contraction of the diaphragm.

(3) Evacuation of the alveolar fluid: discharge through the nose and mouth, drainage through the pulmonary lymphatic system, and resorption through the capillaries.

(4) Reduction of pulmonary vascular resistance following a lessening in arteriolar vasomotor tension, and establishment of pulmonary capillary perfusion (mechanical action of the ventilation and variation of the blood gases).

(5) Adjustment of the circulation, accompanied by disappearance of the right-left shunts of the fetal period.

For 2–3 minutes after the complete birth of the baby, the acid-base balance and the saturation of the venous umbilical blood hardly change; then placental circulation ceases; there is no longer any pulse in the umbilical cord, which should at this point be clamped at the end nearer the infant.

The timetable of respiratory adjustment is as follows:

(1) From the second and third minute of postnatal life and up to about the fifth minute, the pCO_2 rises, the pH is reduced, and the pO_2 remains stationary;

(2) Between 5 and 20 minutes after birth the pCO_2 becomes normal and the pH becomes stabilized above 7.3, indicating efficient ventilation. Only the metabolic component of acidosis persists for several more hours; this varies widely according to individual postnatal conditions, and is responsible for partial respiratory compensation with pCO_2 levels of less than 35 mm Hg.

At the end of the first postnatal hour, the arterial pO_2 is about 60 mm Hg; it rises towards 80 mm after 24 hours of life, and stays at this level for weeks or months. This pO_2 of 80 mm is due to the persistence of an increased right-left shunt and not to unequal ventilation—intrapulmonary perfusion—or to diffusion disorders.

Cardiorespiratory adaptation has been less well studied in the child born before term. It takes place as quickly in the infant born before

term as in the child born at term, provided there is no asphyxia and there is enough surfactant. Nevertheless, in the hours and days that follow, the effectiveness of intrapulmonary gaseous exchange declines in proportion to the immaturity of the infant. Practically all infants born before term (32 weeks or less, with a birth weight under 1800 g) present lung function anomalies, although these are not necessarily manifested in respiratory disorders. Normalization of respiratory function goes hand in hand with postnatal development.

Neonatal asphyxia

This is due to the incomplete adaptation of respiration to the new extra-uterine conditions, either because the respiratory centres do not respond to the various external stimuli (drop in temperature, excitation of the skin) and internal stimuli (hypoxaemia, acidosis) or because an abnormal condition of the lungs prevents effective aeration of the alveoli and/or the establishment of pulmonary perfusion. Any degree of asphyxia between normal establishment and complete failure of respiration may occur.

Respiratory and physiological acidosis present at birth rapidly grow worse, and lactic acidosis due to hypoxia sets in. The cardiovascular system becomes decompensated at a rate depending on the energy reserves present in the myocardium. Since the dysmature infant has only very little glycogen, therefore, it is extremely liable to asphyxia. The cerebral tissue, inadequately irrigated and oxygenated, will be affected to a varying extent, first of all in the regions well supplied with enzymes (basal nuclei, auditory passages, etc.).

This sequence—the non-establishment or arrest of respiration; cardiovascular insufficiency; cerebral lesions—is to be found in all newborn mammals, including man. Thorough experimental studies have been made of the natural history of acute asphyxia (WHO Scientific Group on the Effects of Labour on the Foetus and the Newborn, 1965); in particular, research has made it possible to assess the effectiveness of the different methods of resuscitation.

The newborn infant must make effective respiratory movements during the first, or at the latest the second minute after birth. Various methods have made it possible to assess the child's condition during the first minutes after birth, particularly the effectiveness of cardiorespiratory adaptation. A very widespread method is the Apgar system based on assessment of the heart rate, respiratory effort, muscle tone, reflex irritability, and skin colour at intervals of 1, 5 and 10 minutes after birth.

This examination should preferably be carried out by someone not emotionally involved in the delivery (i.e., a doctor, nurse, or midwife). The Apgar score is useful for drawing general conclusions, for standar-

dizing observation of the newborn, and for assessing the extent of any subsequent decline. It is, above all, a useful starting-point for a prospective study of an asphyxiated baby, but does not suffice in itself to indicate the need for resuscitation. The indications for immediate resuscitation are based on an assessment of respiration (whether present or not; gasping) and on the cardiac activity rate (over 100, less than 100, stable or slowly diminishing).

Resuscitation has two aims:

(1) aeration of the lungs to permit normal establishment of gaseous exchange;

(2) control of cardiovascular insufficiency.

Experimental studies have brought out the essential requirements of intensive resuscitation of the newborn and made it possible to choose between the different techniques available (hypothermia, hyperbaric oxygen, administration of oxygen by the gastric route, administration of analeptics, intubation, and ventilatory assistance). The most effective method is intubation, followed by controlled inflation (maximum 30 cm of water) of the lungs and administration (once the lungs are aerated) of alkalizers (bicarbonate of soda or tromethamine [1]) and glucose. Occasionally, mask ventilation can be tried initially. Resuscitation must be carried out by the most competent member of the obstetrico-paediatric team.

Following asphyxia and resuscitation, complications must be expected:

(1) *Complications of a general nature:* disorder of the blood crasis with subarachnoid or intraventricular cerebral haemorrhage, haemorrhage of the parenchymatous organs, umbilical haemorrhage; metabolic disorders (lactic acidosis, hyperkalaemia, hypoglycaemia, etc.); cardiovascular shock; gastric perforation; infections due to resuscitation activities (otitis, bronchopneumonia, meningitis, septicaemia).

(2) *Respiratory complications:* post-asphyxial respiratory distress on extensive inhalation of amniotic fluid, whether meconial or not, or respiratory distress due to hyaline membrane disease in infants born before term; iatrogenic lesions: pneumothorax, pneumomediastinum.

(3) *Complications of the central nervous system:* immediate cerebral distress of varying intensity and, in particular, permanent neurological sequelae.

The resuscitated infant comes into the high-risk category and must be meticulously observed during the first 4–6 hours after birth to permit

[1] Tris (hydroxymethyl)aminomethane.

the early detection and, if necessary, correction of post-asphyxial complications.

Respiratory distress in the newborn

Respiratory morbidity remains the major problem of the early postnatal period. Up to 10% of all newborn infants, and 40% of those in special care units, present respiratory problems of varying intensity. These problems may account for 70–80% of early neonatal deaths.

Respiratory distress is associated with the following signs: polypnoea at 60 minutes and more (may be absent in infants born before the 32nd week of gestation), cyanosis when the child is in a normal environment, expiratory groaning, and intercostal, suprasternal, and diaphragmatic retraction sometimes accompanied by flapping of the alae nasi.

Respiratory distress has numerous causes: respiratory or cardiac malformations, infectious congenital pneumopathies (amniotic infection, listeriosis, etc.), severe anaemia or pronounced haemic plethora, extensive pulmonary haemorrhage, hyaline membrane disease, post-asphyxial syndrome (extensive inhalation of amniotic fluid, whether meconial or not), and respiratory distress of indeterminate type.

There is some confusion regarding the term "respiratory distress syndrome" (RDS). English-speaking authors use the term "idiopathic RDS" for anything that cannot be included within a known clinical framework (respiratory distress due to malformation, to inhalation of amniotic fluid, etc.), and regard this as in some degree associated with hyaline membrane disease. However, the two terms do not always coincide. By analogy with other clinical situations, it would be wise to keep the term RDS solely for describing the well-defined clinical picture and to add an indication of the cause, e.g., RDS on inhalation of meconial amniotic fluid, RDS due to hyaline membrane disease.

To permit the comparison of morbidity and mortality statistics between countries and even between units, it would be useful to draw a careful distinction between the following terms:

(1) secondary respiratory distress syndromes;
(2) respiratory distress on aspiration (postasphyxial syndrome);
(3) respiratory distress due to hyaline membrane disease;
(4) respiratory distress of indeterminate type;
(5) respiratory distress in newborn of 1000 g or less, or born at 28 weeks or less.

Where possible the treatment of respiratory distress is based on the cause, but more often it is based on the symptoms, particularly in the case of hyaline membrane disease. Here, treatment comprises control of the thermal balance; correction of any metabolic anomaly; control

of the circulation; optimum oxygenation, avoiding both hypoxia and hyperoxia because of the danger of retrolental fibroplasia and cerebral lesions; and lastly, control of superinfection by hospital germs and the control of iatrogenic lesions (the aggressiveness of treatment and hence the frequency of lesions rise in proportion to the immaturity of the infant). The complexity of this treatment calls for the creation of special care units, with some regional centralization.

The disappearance of delivery before term would eliminate hyaline membrane disease, which is closely connected with immaturity. Similarly, the prevention of fetal hypoxia would avoid respiratory distress on extensive inhalation of amniotic fluid.

Recurrent apnoea syndrome in the child born before term

The breathing of newborn infants, especially those born before term, is often irregular with phases of apnoea lasting several seconds (up to 15 seconds). Newborn infants of 30 weeks' gestation or less are often observed to have longer periods of apnoea; these may cause pronounced hypoxia, associated with (often severe) hypercapnia and possibly with hypoxaemic lactic acidosis and cardiovascular repercussions. Repetition of these periods of apnoea can threaten the infant's life and will certainly endanger its central nervous system.

This recurrent apnoea is observed in association with pulmonary disorders (such as hyaline membrane disease), where it indicates that the basic disease is of some severity; with cerebral haemorrhages (usually ventricular, but also subarachnoid haemorrhage of varying extent, particularly peribulbar haemorrhage); or with symptomatic hypoglycaemia, hypocalcaemia, or an infection (meningitis, septicaemia, etc.). Often, however, no cause can be found (functional immaturity of the respiratory centres).

Treatment consists primarily of external stimulation (which calls for constant observation and hence for ample experienced staff), possibly with ventilatory assistance.

Sequelae of hypoxia

The problem of possible neurological sequelae after perinatal hypoxia is an extraordinarily complex one. Many studies show an association between a history of antenatal hypoxia (fetal distress, neonatal asphyxia) and anomalies of psychomotor, intellectual, and social development. Identical conditions have been described in infants underweight at birth or with respiratory distress, postnatal hypoglycaemia, or recurrent apnoea. Admittedly it is impossible to provide

TABLE 8. TYPES OF BIRTH INJURY

Type of injury	Approximate incidence (%)	Causal factors	Sequelae			
			Death	Permanent handicap	Complete recovery after treatment	Insignificant
Intracranial injury						
Tearing of the falx cerebri, tentorium cerebelli, and vena cerebri magna Subdural haematoma Cerebral haemorrhage, laceration, contusion, or oedema Subarachnoid haemorrhage Intraventricular haemorrhage	1	Breech delivery Forceps delivery Immaturity Perinatal asphyxia	Likely	Likely	Possible	Unusual
Fractures						
Skull Spinal column Clavicle Humerus Femur	0.05	Forceps delivery Breech delivery Shoulder dystocia Breech delivery	Likely Unlikely	Likely Unlikely	Possible but unusual Usual	
Paralysis of cranial and peripheral nerves						
Facial nerve	0.1	Forceps delivery Central asphyxia Akinesia algera		Possible	Usual	
Erb's paralysis, Klumpke's paralysis Phrenic nerve Radial nerve Circumflex nerve		Breech delivery and Shoulder dystocia		Usual	Possible	

Lesions of internal organs						
Haemothorax Haemoperitoneum Ruptured liver Adrenal haemorrhage Pneumothorax Perforation of the stomach	0.01	Breech delivery (doubtful) Active resuscitation Intra-gastric oxygen	Likely Possible Likely	Unlikely	Possible Likely Possible	
Lesions of soft tissues						
Caput succedaneum		Established labour Forceps delivery Vacuum extraction				Usual
Cephalhaematoma	1		Unlikely	Unlikely	Transfusion occasionally required	Usual
Fat necrosis	0.05					
Bruises, abrasions, and lacerations		Forceps delivery	Unlikely	Unlikely	Treatment not needed	Usual
Incisions		Caesarean section Fetal blood sampling	Unusual	Unlikely	Treatment occasionally required	Usual
Sternomastoid haematoma	0.05	Birth injury (doubtful)	Unilkely	Possible torticollis	Usual	

After Huntingford (1969) *Birth injuries*. Unpublished working document Euro 0410/12.

definite figures for the incidence, severity, or nature of the neurological sequelae of perinatal hypoxia, for the studies required are beyond the capacity of an ordinary research group and can only be carried out on a multidisciplinary basis. With the decline in perinatal mortality, however, cerebral sequelae and other problems due to pathological events occurring at the end of pregnancy or in the first week after birth are becoming one of the major concerns of health services.

BIRTH INJURY

In practice, for obvious psychological reasons, it is better to speak of birth injury than obstetrical injury. The term is not clearly defined: it may imply local lesions (fractures, haemorrhages) in the newborn infant that are due to external force (obstetrical manipulation) at the time of delivery, or it may cover all pathological lesions occurring at the time of birth, whether there was external violence or not, including both traumatic lesions and lesions related to asphyxia or immaturity.

In the restricted sense, birth injuries have become less frequent in recent years: in the United Kingdom, perinatal mortality due to birth injury fell from 2.87 in 1961 to 2.08 in 1966. The types of lesion that occur and their estimated incidence are summarized in Table 8.

The infants exposed to birth injury are those of primiparae and of multiparae in a fourth or later pregnancy; the children of mothers belonging to less privileged socio-economic groups; the children of unmarried mothers; infants born in a rural area; infants born after a prolonged pregnancy; and infants whose birth weight is too low or too high. Attention should also be drawn to the injuries that may be caused by new obstetric techniques, such as vacuum extraction (haemorrhages in the scalp, with severe anaemia) and blood sampling from the fetal scalp (resulting in severe haemorrhage, etc.).

Prevention involves the following steps: detection of mothers at risk; detection of feto-pelvic disproportion; prevention of intrauterine asphyxia, delivery before term, and prolonged pregnancy; avoidance of such obstetric manipulations as version by internal manipulation, breech delivery, forceps delivery, and vacuum extraction. From all the evidence, these changes will result in an increase in the practice of caesarian section, which would mean better planning of delivery. There is every reason to expect an improvement in the statistics provided that the best possible anaesthetic skills and operative techniques are applied.

CHAPTER 3

ORGANIZATION OF CARE

GENERAL

Some measures for reducing perinatal morbidity and mortality can only be effective over a long period, whereas others can bring more immediate results.

The aims of long-term action are (1) to improve the general health of the population as a whole and the mother-to-be in particular (influence on height, cardiac volume, skeletal structure) through appropriate health measures and a well-balanced diet; (2) to improve social conditions (housing, work, recreation, etc.); and (3) to broaden the base of general education, particularly as regards human biology and reproductive phenomena.

It may take one or two generations for such measures to bear fruit, but in the meantime there are more immediate steps that can be taken to improve obstetric and paediatric care: the organization of the fullest possible pre- and postnatal care; the establishment of new obstetric services and the improvement of existing facilities; the establishment of special services, including intensive care units, for babies at high risk; the improvement of transport facilities; the surveillance of high-risk babies with a view to the early detection of psychomotor anomalies; the introduction of genetic counselling; and the establishment of reference centres.

The organization of a complete health service upsets habits, interferes with established usage and, in particular, comes up against outlooks in conflict with good medical practice. Hence, the planning of care to ensure optimum health for the newborn will vary from country to country, depending on historical, social, and economic characteristics. In many places, well-equipped specialized centres have been available to all for many years, and it is appropriate here to evaluate their effectiveness.

Several authors have drawn attention to the fact that some expectant mothers do not know of or cannot take advantage of existing care

facilities. These are women who belong to under-privileged socio-economic groups and present unfavourable biological features, and are precisely those who are in most need of surveillance and care. All too often, the public health services are organized solely to receive people who come to them, whereas the important thing is to go out to those who do not come but have greater need of services. Very often, too, the large number of services concerned with one person or family results in inconvenience or insecurity. Relations between surveillance and care services and the user should therefore be well planned and reflect a more considerate approach: for example, an expectant mother with several children at home cannot wait for hours at a prenatal clinic. A more authoritarian way of ensuring attendance at clinics is to make it a condition of the payment of allowances, but it is preferable to adopt more subtle measures in which health education plays a large part, and so create genuine motivation for attendance and care.

The information required to evaluate the efficiency of services, although accurate, is often scattered. The problem of obtaining a regular flow of information is particularly acute in the field of prenatal and perinatal care. All the relevant data should therefore be recorded on a personal card kept with the expectant mother and afterwards with the child.

GENETIC COUNSELLING

When genetic counselling takes place at the time of premarital examination, its main purpose is to advise prospective parents and families with a history of malformations or hereditary diseases. It is the responsibility of the paediatrician, and in particular of the neonatologist, to refer parents to the geneticist and to provide the latter with the full clinical history including the results of any pathological examinations. The geneticist will complete these data by making a family investigation and will, if necessary, utilize special procedures such as cytogenetic techniques. With the information obtained he can calculate the risk, in some situations with considerable accuracy but in other cases in more general terms.

Regional or national genetic information centres can be of inestimable value to all geneticists. These centres could maintain epidemiological registers of malformations (WHO Expert Committee on Human Genetics, 1969).

SURVEILLANCE DURING PREGNANCY

The team responsible for the expectant mother consists of the obstetrician, the midwife, the social worker, the public health nurse, the mother-

craft nurse, the physiotherapist, and, in the case of a high-risk pregnancy, a paediatrician competent in neonatology. Surveillance should be methodically organized and should follow a fixed timetable.

Initial examination

The initial examination should take place as soon as suspected amenorrhoea of pregnancy occurs, for it is of the utmost importance to be able to determine the date on which gestation commenced as accurately as possible. This examination can establish:

(1) the mother's socio-biological background; it can be supplemented, if necessary, by a visit or inquiry on the part of the social worker or public health nurse;

(2) the mother's medical history: detection of heart disease, endocrinal disorders (diabetes, thyroid disease, etc.); evaluation of the extent of infection with certain diseases, i.e., tuberculosis, syphilis, rubella and, depending on the area, toxoplasmosis and listeriosis; determination of blood group and the possible presence of iso-immunization;

(3) the mother's gynaecological and obstetric history: clinical and gynaecological condition, if possible with cytological screening for any cervical abnormality or vaginal infections;

During this full examination, the doctor can explain to the mother both the physical and psychological consequences of pregnancy, and can draw her attention to the danger for the fetus of cigarette smoking, unsupervised consumption of drugs, and exposure to various physical agents. Finally, it is advisable to describe the rules of gestational hygiene, particularly the importance of a full and well-balanced diet.

Following this initial examination, the essentials of the anamnesis and the clinical and paraclinical observations are recorded on two copies of a standard card. One copy is given to the mother and the other is kept by the clinic.

Later examinations

Examinations should be conducted monthly until the 28th week, then fortnightly until delivery; in a primipara, weekly examinations may be necessary from the 26th week onward. However, this schedule may be varied according to the mother's health and the course taken by the pregnancy.

These examinations will establish:

(1) the general state of health: physical and mental well-being, haemoglobin rate, cardiac volume, etc.;

(2) the presence of any general disease prior to or revealed by pregnancy;

(3) uterine or fetal growth (twinning, fetal malnutrition, etc.);

(4) the presence of any obstetric complication, e.g., vaginal haemorrhages, pre-eclampsia (excessive weight gain, diastolic blood pressure of 90 mm Hg and above, oedema, proteinuria), clinical or biological signs of any danger of interruption of pregnancy;

(5) the presence of any infection, general or localized (bacteriuria);

(6) the possibility of feto-pelvic disproportion or presentation anomalies.

Throughout gestation, the mother will be prepared for confinement with the help of psycho-physical techniques. Moreover, the mothercraft nurse will initiate her, as well as the future father, in the basic care of the new baby and the problems of the first year.

High-risk pregnancies

These various examinations and observations will permit the early detection of those expectant mothers (about 20%) during whose pregnancy and delivery the fetus may be at high risk. The predisposing conditions of high-risk pregnancies are:

(1) poor socio-economic background;

(2) primiparity or multiparity (from the fourth pregnancy onward);

(3) maternal age of more than 30;

(4) a history of antepartum haemorrhages, perinatal death, or live birth of a child under 2500 g;

(5) haemoglobin rate less than 9.5 g per 100 ml;

(6) diastolic blood pressure above 90 mm Hg (with or without proteinuria);

(7) haemorrhages before the 28th week;

(8) onset of labour outside the full-term period.

As a matter of priority, such expectant mothers should be kept under especially close surveillance.

Prenatal rest

Employment is not in itself a risk factor, but any night work, work in a toxic environment, or work involving tiring travel should be prohibited. In the case of women with an unfavourable socio-biological background, the advisability of continuing in employment should be considered between the fourth and sixth months of gestation.

Generally speaking, every expectant mother should cut down her activities from the 34th week of pregnancy. A household help should

be made available at this period to mothers of large families (more than 3 children) and to mothers with closely spaced young children.

In particular cases (pregnancy disorders with hormonal insufficiency, pre-eclamptic toxaemia, confirmed heart disease, small cardiac volume, danger of premature delivery with haemorrhages or cervical dilatation, or twin pregnancy), rest should begin earlier and should sometimes be complete, not at home but in hospital. In obstetric departments, one rest and observation bed should be provided for every 3–4 delivery beds.

DELIVERY AND RESUSCITATION

The place of confinement may vary from country to country, but in general a well-equipped obstetric ward is recommended. Careful selection of expectant mothers for home confinement (second or third parity, under 30 years of age, and no history of disease) does not necessarily protect them from sudden complications necessitating transport to a centre. Even in the best conditions, such emergency transport following home confinement incurs higher perinatal mortality than hospital confinement. Hospital confinement, however, has two disadvantages: (1) the increased risk of hospital infections and (2) somewhat less personal relationships between the expectant mother, the doctor, and the medical staff, a drawback that is particularly keenly felt in teaching hospitals. Careful organization can counter these disadvantages.

If hospital confinement is recommended, it goes without saying that the medical and paramedical staff and the facilities available should be adequate to meet any situation. No establishment should be officially authorized for service unless it meets the necessary standards.

The obstetrics department should be organized to provide for the continuous observation of the fetus, with adequate equipment, and should be staffed by a multidisciplinary medical and paramedical team, including an anaesthetist and a paediatrician. The paediatrician should be present in the delivery room for every high-risk delivery in case he is needed. An area for resuscitation should be provided in the ward, equipped with a heating appliance. The resuscitation equipment should always be ready for use, and checked on each change of team.

CARE OF THE NEWBORN

Every newborn infant should be carefully observed and examined during the first 10 minutes of extra-uterine life with a view to assessing its maturity in the light of the reported duration of pregnancy, its peri-

natal adaptation (particularly as regards the respiratory system), and the presence or absence of serious malformations or fetal diseases (isoimmunization, infections, repercussions of any maternal disease, especially of endocrinal disorders). This examination should be carried out by a physician or, in his absence, by an experienced medical auxiliary.

The nursery

The nursery is part of the obstetric department, and should be equipped so as to keep the risk of hospital infection as low as possible. Babies kept in the nursery can spend part of the day with their mothers.

Every baby should be seen by the paediatrician or by a doctor competent in neonatology at least once and, if possible, twice in the neonatal period (the first examination during the first 24 hours, the second examination in the 24 hours preceding discharge).

During its stay in the nursery, the infant should be kept under constant observation with particular regard to the following points: early detection and treatment of hyperbilirubinaemia, whatever the cause; check on the establishment of gastro-intestinal function and passage of urine; feeding (early detection of dietary intolerances, etc.); bacterial and possibly viral colonization; careful examination for malformations and metabolic diseases (dislocation of the hip, foot anomalies, anomalies—even minor ones—of the external genital organs, Hirschsprung's disease, hypothyroidism, phenylketonuria, galactosaemia, leucinosis, mucoviscidosis, etc.); evaluation of the central nervous system (hypertension, hypotension, asymmetry, etc.).

Observation unit for high-risk newborn infants

The mother's history, particularly regarding the course of pregnancy, and the results of the examination at birth, will permit the paediatrician to foresee complications, whether early (within 24 hours of birth) or late (more than 24 hours after birth), which may endanger the infant's life. Newborn infants at high risk can easily be identified from the mother's socio-biological characteristics and the history of the pregnancy (Table 9), from the mother's medical history (Table 10), the circumstances of confinement (Table 11), and certain observations made at the time of birth (Table 12).

The high-risk infant, thus defined, requires very close observation, and this is usually impossible in the nursery. A special unit for immediate and constant observation should therefore be provided in the close vicinity of the delivery room; it should have close links with the special care unit and the nursery. Should the circumstances (number of deliveries, staff and equipment available) so require, the observation unit and the special care unit may be combined.

TABLE 9. ASSOCIATION OF SOCIAL AND PHYSICAL CHARACTERISTICS OF THE MOTHER AND DISORDERS OF PREGNANCY WITH INFANTS AT HIGH PERINATAL RISK

Characteristics or disorder of the mother	Risk factor in infant [a]							
	Prema-ture	Birth weight too low	Malfor-mations	Infec-tions	Cerebral lesions	Hypogly-caemia	Hyper-bilirubi-naemia	Types of respiratory distress
General:								
Small stature	+			(+)			(+)	Hyaline membrane disease
Poor socio-economic conditions	+			(+)			(+)	Hyaline membrane disease
Small cardiac volume	+			(+)			(+)	Hyaline membrane disease
History of sterility	(+)	Dysmaturity	+			(+)		
During pregnancy:								
Vaginal haemorrhages	+				+		(+)	
Cervical insufficiency	+			+			(+)	Fetal pneumonia
Toxaemia of pregnancy		Dysmaturity				+		Alveolar haemorrhages
Hypertension > 135 mm Hg		Dysmaturity				+		Alveolar haemorrhages
Hydramnios			+					
Oligo-amnios			+					Pulmonary hypoplasia

[a] + = Frequent association.
(+) = Possible association, less frequent.

TABLE 10. ASSOCIATION BETWEEN MATERNAL MEDICAL HISTORY AND NEWBORN INFANTS AT HIGH RISK

Maternal disorder	Risk factor in infant [a]						
	Prematurity	Birth weight too low	Excessive birth weight	Malformations	Infections	Hypoglycaemia	Diseases of newborn
Endocrine disorders:							
Diabetes, prediabetes	+		+	(+)		+	
Hyperparathyroidism							Hypocalcaemia
Infectious diseases:							
Rubella		+	+ [b]		+		Infection
Toxoplasmosis		+		+ [b]	+		Infection
Cytomegalic inclusions		+		+ [b]	+		Infection
Syphilis		(+)			+		Infection
Listeriosis	+				+		Infection
Bacteriuria	+				(+)		Hyaline membrane disease
Hepatitis B							Neonatal hepatitis
Intoxications:							
Cigarettes		+				+	
Morphine, etc.		(+)					Weaning syndrome
Medicaments				+			
Immunology:							
Feto-maternal incompatibility	(+)					(+)	Specific disease
Auto-immunizing diseases:							
Basedow's disease, Hashimoto's disease, Werlhof's disease, lupus erythematosus							Specific diseases

[a] + = Frequent association.
(+) = Possible association, less frequent.
[b] These are generally pseudo-malformations, i.e., post-necrotic sequelae that may interfere with organogenesis.

TABLE 11. ASSOCIATION BETWEEN DELIVERY ANOMALIES AND NEWBORN INFANTS AT HIGH RISK

Anomaly of delivery	Risk factor in infant [a]							
	Prematurity	Birth weight too low	Asphyxia	Infections	Anaemia	Birth injury	Cerebral lesions	Miscellaneous complications
Breech presentation			+		(+)	+	+	Suprarenal haemorrhages
Caesarian delivery			+		(+)			
Forceps delivery			+	(+)		+		
Vacuum extraction			+		+	+		Scalp haemorrhages
Fetal distress			+			+	+	Hyaline membrane disease; aspiration of amniotic fluid
Second twin		+	+	(+)		+	+	
Premature rupture of amniotic sac	(+)			+				

[a] + = Frequent association.
(+) = Possible association, less frequent.

TABLE 12. ASSOCIATION BETWEEN BIRTH DISORDERS AND NEWBORN INFANTS AT HIGH RISK

Disorder at birth	Risk factor in infant [a]										
	Infections	Respiratory distress			Apnoea	Haemorrhage	Hypoglycaemia	Hypocalcaemia	Hyperbilirubinaemia	Cerebral lesions	Birth injury
		Hyaline membrane disease	Post-asphyxial syndrome	Alveolar haemorrhages							
Birth before term	(+)	+			+	(+)		+	+	+ [b]	
Dysmature				+			+			+	
Birth after term			+								+
Accelerated growth		[c]					[c]				+
Asphyxia			+			+	(+)	(+)	(+)	+	
Hypothermia	(+)			+			+				

[a] + = Frequent association.
(+) = Possible association, less frequent.
[b] Below 1500 g.
[c] If child of diabetic mother.

Surveillance, in the hands of qualified nurses who may have access to electronic monitoring apparatus, will be concerned with the respiratory system (respiratory distress syndrome, apnoea, etc.), the cardiovascular system, the central nervous system (convulsions, etc.), and with the evacuation of the first meconium and the first micturition. Clearly such surveillance can only be carried out properly under special conditions, with the naked infant placed in an incubator. Besides the points listed above, a watch is kept for signs of fetal diseases or the presence of malformations. If necessary, preventive treatment can be initiated.

Advantage is taken of this period of observation to compile a record for the infant containing obstetrical information, a description of the first 10 minutes following birth (time of first cry, Apgar score, development of the heart rate, number of bradycardiac phases, etc.), and the clinical signs observed. This record should always remain with the child. It is essential for assessing the baby's development and condition, both immediately and at later stages.

Within 4–6 hours the condition of the baby (and in particular its cardiorespiratory system) will have become sufficiently clear to permit a decision as to whether to place it in a normal nursery or in a special care unit. In the latter case, it should be taken there, together with its record and a sample of maternal blood, by a member of the paediatric team (see Fig. 5).

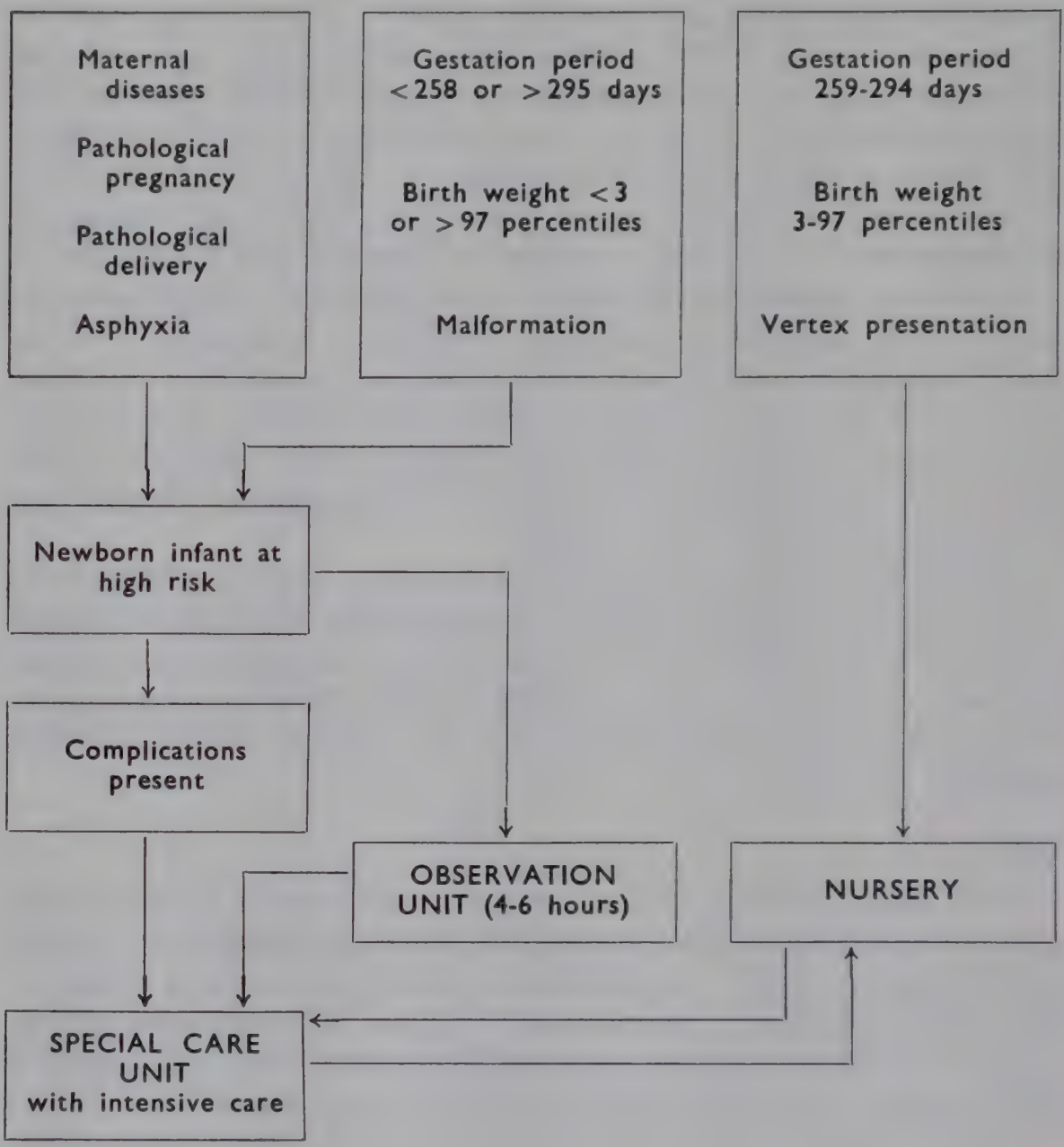
Special care unit

This unit will be responsible for dealing with all the problems that arise during the neonatal period and for the special nursing care needed by before-term babies. Organizational details are shown in Annex 4. The strict application of simple rules of hygiene will enable the unit to accept both infected and non-infected babies from different hospitals, and thus make more economic use of staff and equipment.

The unit should be run by a paediatrician specializing in neonatology and working in close collaboration with the obstetric and paediatric departments. Depending on local conditions, it will be located in one or the other of these departments or, better still, between the two.

The unit should have access to radiological equipment and to a laboratory employing micromethods for determining blood gases, acid-base balance, electrolytes, etc.; it should be in close contact with a haematological and serological laboratory (for determining blood group, antibodies, exchange transfusion, immunoglobulins, etc.) and with a bacteriological and virological laboratory. There should be round-the-clock biological surveillance. Both the collection of information (results of different dosages, etc.) and the communications circuit should be organized systematically.

FIG. 5. ORGANIZATION CHART FOR THE SPECIAL CARE UNIT, THE OBSERVATION UNIT, AND THE NURSERY



There will be close collaboration with the surgeon. Facilities should be available within the unit for certain common surgical procedures, such as taking intravenous, intra-arterial and intragastric samples, transfusions and exchange transfusions, gastrostomy, and peritoneal dialysis.

Infants that have been cured, or no longer require special nursing care, are transferred to the nursery or sent home. Before sending a child home it may be necessary to investigate the social background, and it is important for the mother to be given speedy training in baby care (several hours a day for 2–3 successive days).

Transport of newborn infants at high risk

The transport of babies born before term or of those suffering from respiratory, circulatory or metabolic complications, is a difficult and largely unsolved problem. The transport incubators at present in use are not satisfactory. It would be useful to study, in a European context, the development of a vehicle specially designed for this purpose.

Wherever possible, it would certainly be preferable to transport the mother beforehand to a place with appropriate facilities for the care of such infants. However, a certain number of high-risk infants—those born before term and those unexpectedly presenting some serious complication or malformation—will always have to be transported.

Transport should be prepared, organized and carried out by the special care unit. This unit should equip the vehicle and provide a nurse to accompany it; if circumstances so require, a second nurse and a doctor should also be made available. Because of the need to initiate treatment and special care as early as possible, the vehicle must fulfil a certain number of conditions:

(1) It must be spacious enough to enable two to three persons to move freely around an open bed provided with a heating appliance or incubator.

(2) A newborn infant with respiratory disorders (the most frequent and serious emergency) will be suffering from or in danger of hypoxia, and will therefore be very sensitive to changes of position. Consequently the vehicle's suspension should be very carefully designed so as to eliminate jolting or reduce it as far as possible. If this is done, transport will no longer be a matter of urgency and the vehicle will not need to be capable of very high speeds.

(3) The vehicle's equipment should be similar to that of a static intensive care unit: 8–10 electrical points, 2–3 hours' supply of hot and cold water, oxygen, including all the facilities for optimum conditioning (temperature, humidity), and adequate lighting for accurate work.

(4) Facilities should be available for arterial and venous blood sampling, transfusion (and, under exceptional circumstances, exchange transfusion), intubation, and artificial ventilation.

(5) Depending on the hilliness of the country and the density of the traffic, the distances to be covered will vary at different places and different times. If the time required at cruising speed is more than one hour, the vehicle should be equipped with laboratory facilities for the determination of acid-base balance, haemoglobin, saturation rate, and glycaemia.

CARE OF THE MOTHER AFTER DELIVERY

Besides medical supervision proper, which includes the prevention of iso-immunization, the mother should repeatedly be told exactly what are the advantages of breast-feeding, why it is needed, and how to care for her baby. Every normal nursery and every special care unit should have qualified staff and the necessary accommodation for teaching mothercraft unhurriedly and according to the mother's educational level. If the child presented neonatal complications or malformations, the problems should be discussed on several occasions with the mother and father, and once the first emotional reactions have been overcome a plan of action should be worked out. Where necessary, the advice of a geneticist should be sought.

Lastly, the obstetrician should raise the question of further pregnancies, stressing the importance of a good understanding of family planning and carefully explaining the different methods of birth control. Where the mother is at increased risk—for example, is she has already had three or four children and is approaching 35—the dangers of a further pregnancy should be clearly pointed out; ways of avoiding it should be discussed with the couple, who should choose the method that suits them best.

POSTNATAL SURVEILLANCE OF THE INFANT AT RISK

The possibility of a cerebral lesion is always at the back of the obstetrician's or paediatrician's mind. However, not all cerebral or sensorial lesions are clinically evident during the neonatal period, and paraclinical examinations are not applicable in all cases. Periodic examinations carried out according to a now well-established schedule would no doubt bring anomalies to light more often and even indicate their significance for the child's future (WHO Regional Office for Europe, 1967), but this type of investigation is still not common enough.

The ill effects of cerebral lesions would appear to depend on the time of detection and of initiation of treatment—generally symptomatic treatment—and on the socio-economic background of the family, particularly the mother. It is therefore essential not to lose sight of children who have shown signs of brain damage in the early neonatal period or are suspected of having such lesions or of having belonged at any time to the high-risk category.

The obstetrician in charge of prenatal supervision and delivery and the paediatrician of the special care unit are jointly responsible for placing the infant on the register of children at high risk, thus setting

in motion an administrative process which may at times have unforeseeable consequences. Obstetricians and paediatricians should therefore consider fully the implications of their decision and discuss the matter thoroughly with the parents.

In the interests of these children, effective surveillance should include the following steps: entry in the register of children at high risk; establishment of a central card index and communication of its contents to a medical team; regular check-ups; preparation, in consultation with the parents, of a plan of action whose operation should be regularly checked; and establishment of the facilities for diagnosis, treatment, and education required for different types of handicap.

The ease with which this postnatal surveillance can be instituted will depend on whether the health services in the country concerned are state-run, with clearly defined regional networks, or are organized on the basis of comparatively free and individual medical practice. In either case, the standard of care can be excellent, but it will be more difficult to ensure continuity of surveillance and case-finding where medical practice is entirely liberal.

REGISTERS OF NEWBORN INFANTS AT RISK

The establishment of a register for newborn infants at risk may give rise to certain difficulties (Thomas, 1968):

(1) What types of newborn should be registered? Three high-risk groups may enter into consideration: (*a*) those with a definite lesion or malformation; (*b*) those with a probable lesion or malformation; and (*c*) those who have experienced situations exposing them to potential risks. The danger with this type of register is dilution—in other words, inflated lists due to the notification of a great number of cases, with the result that the child in real danger is lost to view. Under these and other circumstances, it is necessary to draw up a list of priorities corresponding to the practical possibilities of case-finding and treatment. It is in this context that selection should be made.

(2) Should registration be automatic (on the basis of the birth certificate, for example) or should it be made on a separate card during the first week after birth? The registration of the infant at high risk can be regarded as a method of compiling epidemiological statistics or as a surveillance measure aimed at the early detection and treatment of children threatened by a handicap. In the latter case registration can be only individual, not automatic, and should take place on the sole responsibility of a doctor.

(3) Will registration of a newborn infant at risk alarm parents unnecessarily? The parents' reactions will depend on their socio-economic background and on the doctor's tact. In general, the birth of a child in abnormal conditions, either before term or after a disturbed pregnancy or confinement, worries the parents; in such cases the registration of the baby and the establishment of a plan of action is evidence of the doctor's interest and ability to reach a decision, and consequently it reassures rather than alarms the parents.

It should be stressed that a special register is not an end it itself, but implies the existence of basic medical and educational services that can ensure optimum conditions of case-finding and treatment for the infant who may have a handicap.

EVALUATION

Like any other undertaking, the work of the obstetric-paediatric team should be subjected to continuous evaluation. At weekly or fortnightly case conferences attended by the entire medical and paramedical team, all cases of perinatal mortality and morbidity should be discussed in order to determine whether and how they might have been avoided—not so as to criticize this or that member of the team, but so as to re-evaluate the standard of surveillance and care and the appropriateness of medical decisions taken from the moment the mother came under supervision until the observation of the newborn child is completed.

In cases of death, meticulous pathological examination of the infant and placenta by a pathologist competent in perinatal problems is essential to ensure an accurate diagnosis and to reach a better understanding of the circumstances that led to death. This examination should therefore be compulsory in all cases of perinatal death. It is important that the doctors responsible for postnatal surveillance should be associated with this aspect of evaluation. While the paediatrician has a role to play in prenatal supervision of the expectant mother, the presence of the obstetrician is essential during visits to the special care unit for the newborn and in teams responsible for subsequent surveillance of the child. Indeed, in the absence of the obstetrician, mental and psychomotorial development anomalies of all sorts are all too often put down to a perinatal accident. Conversely, observation of the child's development provides the obstetrician with useful information that can help and guide him in his obstetrical technique.

In the light of this continuous evaluation, an inexorable index for which is the total number of perinatal deaths, the training of medical and paramedical staff can be constantly reviewed so that any necessary

changes can be made and, in particular, refresher courses given as required.

The prevention of perinatal accidents calls for collaboration by qualified staff from different disciplines, who are often very difficult to recruit. In every country there is a chronic shortage of doctors and, particularly, of specialized nurses. This shortage, coupled with the rapid development of surveillance and of diagnostic and therapeutic techniques, necessitates periodic re-evaluation of the best distribution of work and responsibilities. Procedures that were regarded as advanced several years ago have now become routine, and can be carried out by auxiliaries without high-level qualifications, thereby freeing staff with a high level of technical training for other tasks. Such constant change calls for adaptability on the part of both staff and administrators, and such adaptability is at present all too rare in the medical and hospital world. Care should therefore be taken not to lay down once and for all the channels of vertical and horizontal co-ordination within or between services, since this co-ordination will need to be modified to meet supply and demand.

CHAPTER 4

INFORMATION, TRAINING, AND RESEARCH

INFORMATION

The mother's (and the family's) socio-biological characteristics and certain extrinsic factors (cigarette consumption, interruption of previous pregnancies, etc.) are of such great importance for perinatal morbidity and mortality that the public at large should frequently be informed by judicious use of modern audiovisual techniques. Information programmes should not exploit the sensational side of the problem, but should be designed to make preventive action both popular and effective.

In the first place, the teaching of biology to children needs to be revised. During the long period of schooling that is customary in most European countries, the time devoted to biology is too short and too often taken up with rather old-fashioned exercises in "natural history". Recent progress in biology has highlighted phenomena that are of importance to every individual. A knowledge of the major functions of the animal organism, and more particularly of the human body, is no longer the preserve of the medical profession but should be within the reach of all.

The problems of human reproduction can be introduced quite naturally into a thoroughgoing study of biological, biochemical, and physiological phenomena at school. Sex education, in its social as well as its biological and technical aspects, forms part of a complete educational programme dealing with pregnancy and the formation of the embryo and fetus as well as with more specific problems, such as family planning, the dangers of exogenous factors for the fetus, and the dangers of abortion. In this connexion, it would be useful for doctors and public health authorities to have their say in the planning of school curricula.

TRAINING

The training and work of the paediatrician and obstetrician have been studied at the Symposium on the Role of Obstetricians in Maternal

and Child Health Programmes (WHO Regional Office for Europe, 1965a) and at the European Conference on Paediatric Education (WHO Regional Office for Europe, 1965b). Since then, the problem of perinatal mortality and morbidity in Europe has assumed even greater importance.

In view of recent developments in both research and practice in this field, training programmes for the medical and paramedical professions need to be revised.

Undergraduate medical training

Traditional and new knowledge on the physiology of the fetus and the newborn should be included in the general course on physiology, which is still all too often focused entirely on the adult. With regard to the introduction of genetics into the medical curriculum, the recommendations made by the WHO Expert Committee on Human Genetics (1962) are still valid and recent developments in this discipline make them even more urgent.

The importance of statistics and data processing in medicine is now generally accepted, but some words of warning should be given against exclusively utilitarian teaching in these new subjects. The important thing is not simply to teach a few set techniques, but rather to impart to the students the intellectual methodology of these subjects, which justify the use of the computers that are now revolutionizing even the most traditional forms of clinical medicine.

In obstetrics, the idea of making each physician an expert at delivery should be abandoned. The practical exercises in obstetrical manipulations could usefully be replaced by a broader study of biology, pregnancy, and fetal growth. The same change should be made in the teaching of paediatrics, where neonatology should be taught systematically, preferably in association with obstetrics. In the basic training of every doctor, the time allocated to neonatology should be between a quarter and a third of that devoted to paediatrics. The social aspects of paediatrics should be brought more to the fore. It is not so much a matter of introducing a new branch of theoretical sociology, divorced from its context, as of getting the student out of the hospital and into the family to share the problems created for the family by a pregnancy, a handicapped child, and so on, under the joint supervision of the sociologist, the paediatrician, and the obstetrician.

Training of the obstetrician

For centuries, the mechanical aspects of delivery have been at the centre of attention. In the past few years, however, a more general

biological approach has emerged, and this should be reflected in the training of the future obstetrician. It should mean more thorough teaching in anaesthesiology and resuscitation, and some 6 months' practical experience in a special care unit for the newborn, where the student will also learn about the problems of handicapped children. Lastly, the preventive and social aspects of obstetrics at each stage of development should be stressed.

Training of the paediatrician

The growing importance of neonatology for paediatrics as a whole should be reflected in the training of the paediatrician: one-thrid of his training at the hospital and outpatient clinic should be devoted to this aspect of his work. Techniques of resuscitation should be studied and practised, as should the neurological examination of the newborn infant and the various techniques of detection. Like the medical student, the future paediatrician should spend more time working outside the hospital, if possible in co-operation with the sociologist. For the paediatrician who wishes to specialize in neonatology, practical training in the delivery ward and in the prenatal care services is essential.

Training of the general practitioner

Since it is one of the general practitioner's duties to conduct deliveries, his training must of necessity take him to the obstetrics ward, the resuscitation unit for infants with asphyxia, and to the special care unit. He should also become familiar with methods of detection and be initiated into the problems of postnatal care. This is particularly important in countries where medical practice is on a private and liberal basis, and the general practitioner plays the major role in detection and prevention.

Further training

The rapid development of perinatal medicine calls for refresher courses for general practitioners, paediatricians, and obstetricians. The acquisition of specific technical skills (intubation, ventilatory assistance, etc.) also requires the organization of practical courses. The importance of medical decisions and of the techniques used during delivery, both for the mother and for the infant, makes constant training necessary. The problem of the doctor who seldom performs deliveries should be reviewed, and postgraduate training should be reorganized so that its benefits reach the medical profession as a whole.

Midwives and paediatric nurses

These personnel provide indispensable assistance in the observation of the mother, the fetus, and the infant. Their training in symptomatology should be very carefully planned. The curriculum should include an introduction to genetics, a broad study of the biology of pregnancy, of the fetus, and of the process of adaptation of the newborn to extrauterine life, and a thorough initiation in the problems of sociology, including family planning. In view of their role in supervising the expectant mother and the child, they should be introduced as fully as possible to case-finding methods and to the social and preventive aspects of this work. The growing importance of teamwork raises the problem of practical activities (for example, the study of a family) undertaken jointly by the student midwife, student nurse, and medical student.

Lastly, there is clearly a need for compulsory refresher courses and continuing education, particularly for nurses and midwives taking up their work again after some months' or years' interruption.

RESEARCH

Medical research in recent years has made very important progress in certain fields of neonatology, including pulmonary, metabolic, and thermal adaptation. The findings almost immediately found practical application in the care and treatment of the newborn. In the hope of seeing similar progress made in the years to come, it would seem wise to undertake theoretical and practical studies along the following lines:

(1) Studies of families in which congenital anomalies have been observed and surveys of twins on a European basis; this would make possible a more accurate estimate of the incidence and particularly the geographical distribution of certain malformations, as well as of the mode of transmission and the environmental factors that may influence them.

(2) In the absence of any deeper understanding of the mechanism that induces delivery, it is difficult to identify the causes of before-term delivery or of prolonged pregnancy. It is certain that a bigger research effort in this field would very soon bring to light useful data for the prevention of these two pathological conditions;

(3) A better classification of the newborn has made it possible in recent years to obtain a better grasp of the phenomenon of placental insufficiency and its corollary, fetal malnutrition. More far-reaching studies, anatomical and biochemical as well as physiological, are still needed for an understanding of the pathological mechanisms governing these anomalies of the placenta and fetus;

(4) Until such time as preventive medicine can eliminate before-term deliveries and intrauterine hypoxia, the study of the child born before term and of the asphyxiated newborn should be continued, especially from the standpoint of cerebral maturation and of the influence of immaturity and asphyxia on blood coagulation. The perfection of an oxygenator with extracorporeal circulation would perhaps enrich the limited resources for the treatment of hyaline membrane disease.

CHAPTER 5

CONCLUSIONS

A number of important points emerge from the preceding chapters. They can be summarized as follows:

1. *Perinatal mortality is affected by the following factors:*

(*a*) the way in which statistical data are collected;
(*b*) the mother's socio-biological characteristics;
(*c*) the frequency of before-term and after-term deliveries;
(*d*) the number of low-birth-weight babies;
(*e*) the organization and standards of obstetric and paediatric care.
(*f*) in the long run, the health status of the population as a whole;

2. Important *medical advances* have taken place in recent years. At the practical level they are reflected in diagnosis and treatment and in the care of both mother and newborn, in the following ways:

(*a*) prevention of maternal sensitization in the event of rhesus incompatibility;
(*b*) antenatal diagnosis of fetal distress due to hypoxia;
(*c*) elucidation of the principles of resuscitation of the asphyxiated newborn infant;
(*d*) improvement of the basic care of before-term babies and of the treatment of newborn with respiratory distress.

3. The *organization* of care in the field of maternal and child health should be reviewed periodically in the light of the special features of each country, bearing in mind:

(*a*) the need to supervise all expectant mothers;
(*b*) the early detection of risk factors in both woman and child, so that prevention and treatment can be conducted properly.

Moreover, prenatal care must be imaginatively designed to anticipate the needs of an entire stratum of the population that does not benefit from the existing facilities.

The authorities, public opinion, and the medical profession should be brought to regard the resources devoted to maternal and child health as a social and economic investment of cardinal importance.

4. In view of their importance for *prevention*, the following points should be given *immediate consideration:*

From the medical standpoint:

(*a*) adequate production of anti-D immunoglobulins to immunize all primiparae, and subsequently all women at risk of sensitization;

(*b*) the review, in many countries, of policy on the legal interruption of pregnancy;

(*c*) a stronger campaign against cigarette smoking, particularly during pregnancy, with the active and convincing participation of the medical profession;

(*d*) vaccination of women against rubella, starting with women at risk (medical and paramedical personnel, teachers) and continuing with other population groups.

From the hospital and administrative standpoint:

(*a*) establishment of sufficient intensive care units for before-term infants and infants at risk to meet the demand;

(*b*) organization or improvement of transport for the newborn;

(*c*) continuity of medical information concerning each pregnancy and each newborn infant, with the possible establishment of registers for newborn at risk;

(*d*) standardization of registration procedures for fetal and neonatal deaths in the different countries of the European Region.

5. Special medical and social endeavours should be made on a *long-term* basis to achieve the following aims:

(*a*) prevention of before-term or after-term delivery;

(*b*) prevention of placental insufficiency and intrauterine hypoxia;

(*c*) epidemiological morbidity surveys and genetic studies on a broader scale, covering the entire population of various countries and even expanded to cover the whole of Europe.

6. *Medical teaching* at all levels should take into account advances in perinatal medicine:

(*a*) broadening of basic education on pregnancy and on the development of the fetus and the newborn infant;

(*b*) a more satisfactory distribution of duties between midwives and doctors, and between doctors of different disciplines; this would no

doubt entail a reduction in the number of persons qualified to conduct a delivery, but their training would benefit;

(*c*) the general teaching of the basic knowledge and skills of resuscitation as a whole, and especially resuscitation of the newborn;

(*d*) more thorough teaching of perinatal medicine, both in obstetrics and paediatrics.

Annex 1

DEFINITIONS, RECOMMENDATIONS, AND PROPOSALS CONCERNING THE STATISTICS OF PERINATAL MORBIDITY AND MORTALITY

A. DEFINITIONS AND RECOMMENDATIONS

1. *Definitions adopted by the World Health Assembly* [1]

1.1 *Live birth*

" Live birth is the complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of the pregnancy, which, after such separation, breathes or shows any other evidence of life, such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles, whether or not the umbilical cord has been cut or the placenta is attached; each product of such a birth is considered live born. "

1.2 *Foetal death*

" Foetal death is death prior to the complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of pregnancy; the death is indicated by the fact that after such separation the foetus does not breathe or show any other evidence of life, such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles. "[2]

1.3 *Causes of death*

"The causes of death to be entered on the medical certificate of cause of death are all those diseases, morbid conditions or injuries which either resulted in or contributed to death and the circumstances of the accident or violence which produced any such injuries."

1.4 *Underlying cause of death*

"The underlying cause of death is (a) the disease or injury which initiated the train of events leading directly to death, or (b) the circumstances of the accident or violence which produced the fatal injury."

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[1] World Health Organization (1967) *Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death, 1965 revision*, Geneva, vol. 1, p. 469.

[2] The International Conference for the Eighth Revision " recognized the difficulties encountered in many countries in the practical application of the criteria of 'evidence of life' in the WHO definition of foetal death... It was impossible to ensure that all birth attendants did in fact strictly apply the definition, but these criteria were intended as a guide to them in their decision as to whether a child was born alive or dead. Taking also into account the scant response from countries in respect of a change, the Conference did not see any useful purpose in amending the definition ". *Ibid.*, p. XXVI.

2. *Definition adopted by the International Conference for the Eighth Revision* [1]

2.1 *Perinatal period*

The perinatal period is that which extends "from the 28th week of gestation to the seventh day of life".[2]

3. *Practical definitions occurring in the Eighth Revision of the International Classification of Diseases*

3.1 *Abortion* (640-645) [3]

Categories 640-645 include "any interruption of pregnancy before 28 weeks of gestation with a dead foetus".

3.2 *Delivery* (650-662) [4]

Categories 650-662 include:
"full-term delivery of live- or stillbirths
premature delivery of livebirth
delivery of dead foetus after 28 weeks of gestation."

4. *Definitions recommended by the Statistical Commission of the United Nations*

4.1 *Gestational age* (of child or dead foetus) [5]

"Gestational age (of child or dead foetus) is the interval in completed weeks which has elapsed between the first day of the last menstrual period of the mother and the date of her delivery, irrespective of whether the product of conception was live-born or without evidence of life."

4.2 *Weight* [6]

"Weight of a live-born child at birth or of a dead-born foetus at delivery should be the weight determined immediately after delivery, and should be expressed in grammes to a degree of significance which will allow a classification of 500-gramme intervals to be made."

5. *Recommendations for the establishment of statistical tables of live births and foetal deaths*

The Subcommittee on the Definition of Stillbirth and Abortion set up by the WHO Expert Committee on Health Statistics made the following recommendations:[7]

(1) *Live births*

"Tabulation of all live births, irrespective of the period of gestation, by all countries, with at least the following groups:

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[1] World Health Organization (1967) *Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death, 1965 revision*, Geneva, vol. 1, p. XXVII.

[2] "While agreeing that these were practical limits for international purposes, the Conference noted that some countries extended the collection of pertinent data down to the 20th week of gestation and up to the 28th day of life, preparing tabulations for both the restricted and the wider period. The Conference considered that such extensions should be encouraged..."

[3] World Health Organization (1967) *Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death, 1965 revision*, Geneva, vol. 1, p. 243.

[4] *Ibid.*, p. 244.

[5] United Nations, Economic and Social Council (1968) *Recommendations for the improvement and standardization of vital statistics: draft proposals*, New York, p. 44 (Unpublished document E/CN.3/388/Add.1).

[6] *Ibid.*, p. 54.

[7] *Wld Hlth Org. techn. Rep. Ser.*, 1950, No. 25.

Less than 20 completed weeks of gestation ..... *Group I*
20 completed weeks of gestation but less than 28 ..... *Group II*
28 completed weeks of gestation and over ..... *Group III*
Gestation period not classifiable in groups I, II, and III ..... *Group IV*
(The period of gestation is measured from the beginning of the last menstruation)"

(2) *Foetal deaths*

(*a*) "Tabulation of all foetal deaths is a desirable goal and should be attained as soon as possible."

(*b*) "As a minimum all countries should register and tabulate all foetal deaths occurring after the 28th completed week of gestation."

(*c*) "The following groups should be used in tabulations of foetal deaths:
Less than 20 completed weeks of gestation ..... *Group I*
20 completed weeks of gestation but less than 28 ..... *Group II*
28 completed weeks of gestation and over ..... *Group III*
Gestation period not classifiable in groups I, II, and III ..... *Group IV*
(The period of gestation is measured from the beginning of the last menstruation)
Foetal deaths, group I, may also be described as 'early foetal deaths'.
Foetal deaths, group II, may also be described as 'intermediate foetal deaths'.
Foetal deaths, group III, may also be described as 'late foetal deaths'."

B. PROPOSALS PUT FORWARD BY THE SEMINAR

1. *Conclusions and proposals concerning birth weight*

It was agreed that birth weight was the only criterion suitable for international comparisons, and that infants weighing 2500 g or less were considered in the European Region to be of insufficient weight.

It is desirable that the exact birth weight in grams should be given for each infant in order to facilitate tabulation in accordance with the following groups: 0-500; 501-1000; 1001-1500; 1501-2000; 2001-2500; 2501-3000; 3001-3500; 3501-4000; etc. [1]

It was proposed that products of conception expelled or extracted from the mother and weighing 1000 g or less should at least be recorded separately.

2. *Proposals concerning gestational age*

It is desirable to express gestational age in days for each case. Tabulations should include at least the following groups:

Group I Early fetal period : less than 140 days (20 weeks)
Group II Intermediate fetal period: 140–195 days (20–27 weeks)
Group III Late fetal period : 196 days (28 weeks) and over

It was proposed that the following groups should be added:

"Birth before term": less than 259 days (37 weeks)
"Birth at full term": 259–293 days (37–41 weeks)
"Birth after term" : 294 days (42 weeks) and over

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[1] This subdivision has already been recommended (see *Wld Hlth Org. techn. Rep. Ser.*, 1961, No. 217).

3. *Proposal concerning birth weight and gestational age*

It is desirable to study the relationship between these two criteria and to take them into account in establishing the following groups in each country:

Infants with normal fetal growth
Infants with retarded fetal growth
Infants with accelerated fetal growth.

Annex 2

DEMOGRAPHIC DATA TO BE COLLECTED ON LIVE BIRTHS AND LATE FETAL DEATHS *

	Live birth	Fetal death
Characteristics of the event		
Attendant at birth	+[a]	
Cause of death		+
Certifier or attendant		+
Date of occurrence (delivery or expulsion of the fetus)	+[a]	+[a]
Date of registration	+[a]	+[a]
Gestational age	+	+[a]
Place of occurrence (hospital, private home)	+	+
Legitimacy status	+[a]	+[a]
Place of occurrence (geographical)	+[a]	+[a]
Sex	+[a]	+[a]
Type of birth (i.e., simple or multiple issue)	+[a]	+[a]
Weight at birth or weight of expelled fetus	+	+
Characteristics of mother and father		
Age	+	+
Total number of children born alive to the mother	+[a]	+[a]
Total number of children born alive to the mother and still living	+[a]	+[a]
Total number of children born dead to the mother	+[a]	+[a]
Children born alive to the mother during the preceding 12 months	+[a]	
Children born alive to the mother during the preceding 12 months and still alive	+[a]	
Nationality	+	+
Date of birth; if not available, age	+[a]	+[a]

* Source: United Nations, Economic and Social Council (1968) *Recommendations for the improvement and standardization of vital statistics: draft proposals*, New York, pp. 30-33 (Unpublished document E/CN.3/388/Add.1).

[a] Regarded as taking priority in the United Nations draft proposals.

	Live birth	Fetal death
Characteristics of mother and father (continued)		
Date of marriage or duration of marriage (for legitimate births)	+	+[a]
Duration of residence in usual (present) place	+	
Educational attainment	+	+
National or ethnic group	+	+
Industry	+	+
Interval since last previous live birth to mother	+	
Literacy status	+	+
Occupation	+[a]	+[a]
Place of birth (geographical)	+	+[a]
Place of previous residence	+	
Place of residence at a specified time in the past	+[a]	
Place of usual residence	+[a]	+[a] (mother)
Status (employer, employee, etc.)	+	+

Annex 3

HOSPITAL HYGIENE AND THE PREVENTION OF NEONATAL INFECTION

Every newborn infant, well or sick, should be kept in its own bacteriological and viral microclimate. Different microclimates should not be allowed to come into contact with each other. Each infant should be cared for in a place intended for it alone (bed, incubator, cradle), the medical and paramedical staff and the mother wearing a special overall (changed at regular intervals) for each child.

The air. This should be bacteriologically filtered, suitably warmed and humidified, and pumped into the room by laminar flow ventilation (avoiding eddies); it should be renewed several times each hour, depending on the size of the room and the number and category of infants present. It is better not to return air already used. Ultraviolet rays have not yet been shown to be effective.

Hands. The hands are the most important vectors in propagating hospital infections. They should be rinsed before touching a healthy or sick infant. Since this frequent washing should not be allowed to undermine the natural skin surface, brushes and any aggressive soap or disinfectant should be prohibited. Some of the substances now in use, such as hexachlorophene on its own, are active against only a part of the natural flora of the hands; the resulting imbalance may permit other flora, generally Gram-negative, to develop and cause a hospital epidemic.

Wearing a mask. This is a dangerous practice, and it is impossible to get staff to wear a mask 24 hours a day. It is better therefore to abandon it. On the other hand, staff should be instructed to wash their hands each time they come into contact with the face and naso-oropharyngeal cavities (—penicillin-resistant *Staphylococcus aureus* is present in 30% of medical and paramedical staff). In the event of viral infection, wearing a mask is of no use. Any member of the staff with a virus infection should if possible be kept away from the department while the illness lasts.

Dress. The value of a cap and the soundness of the traditional dress should be thoroughly assessed.

Linen. Linen and other material coming into contact with the newborn should be as sterile as possible. The preparation of batches of material or linen wrapped in paper (permitting risk-free transport) and autoclaved can be arranged at a common centre for the whole hospital.

Resuscitation equipment. Masks, tubes, ventilators, etc. are particularly difficult to sterilize, and often carry *Pseudomonas aeruginosa*. They should therefore be cleaned and very carefully sterilized, possibly using gas.

Feeding. Bottles, teats, and the milk itself may be vectors of hospital infection. The use of liquid milk and throw-away utensils will make it possible, under certain

circumstances, to simplify the problem of feeding the newborn and to eliminate milk kitchens. It goes without saying that breast-feeding by the mother under careful supervision should be encouraged wherever possible.

Sanitary installations. Any damp place in the hospital is colonized by certain Gram-negative germs, particularly *Pseudomonas aeruginosa:* danger points include overflows and sumps in basin waste-pipes, air and oxygen humidifiers in incubators and elsewhere. Sanitary installations and all items of equipment should be designed to overcome these problems.

Bacteriological checks. Each nursery and each unit for newborn infants, whether sick or not, should be given a bacteriological examination once or twice every month (if necessary once a week); this should include air sampling, checks on equipment and damp areas, and possibly checks on the hands and rhinopharynx of medical and paramedical staff. It is essential to display the results publicly for the information of everybody working in the department. The results should be collected by a specially appointed nurse familiar with the problems of hospital hygiene and registered in case an epidemic should occur in the department.

Annex 4

ORGANIZATION OF A SPECIAL CARE UNIT FOR NEWBORN INFANTS

1. *Purpose: polyvalent care unit for:*

(*a*) pre-term babies requiring special supervision and nursing care (usually with birth weight of 2000 g or less;

(*b*) newborn infants at risk, with one or more neonatal complications; hospitalization age: 0–27 days (in some cases 0–6 days).

2. *Care provided*

(*a*) special nursing care (if necessary in incubators);

(*b*) intensive care (ventilatory assistance, continuous observation with or without electronic surveillance, exchange transfusions, peritoneal dialysis, etc.);

(*c*) functional check-ups (detection of metabolic disorders, etc.).

3. *Person in charge*

A paediatrician with training in neonatology, resuscitation (if possible with extensive physiological and biochemical knowledge), and hospital hygiene.

4. *Location*

In general, the unit should be attached to the paediatric department; however, if there are enough deliveries, e.g., 8 000–10 000 per year, it might be attached to the obstetrics department. In any case, close contact should be maintained with the obstetrics department.

Liaison should be maintained with the infant surgery department, blood transfusion unit, and laboratory services.

5. *Size of unit*

In order to economize and concentrate highly qualified staff and the equipment, which often calls for delicate handling, it is helpful to centralize the facilities for each region so that each centre deals with the special problems occurring in roughly 10 000 births.

10 000 births per year:

3% newborn of 2000 g or less	300
4% newborn of 2000-2500 g, half of whom will present problems ...	200
newborn over 2500 g, of whom 3% present problems	300
	800

800 newborn per year, with an average stay in hospital of 2 weeks, amounting to 1600 weeks per year = 30 beds.

30 beds + a reserve of $\frac{1}{3}$ to cope with unevenness in length of stay = 40 beds, of which 10–12 should be incubators and 3–4 should be intensive care beds (with or without incubators).

6. *Supply circuits*

(*a*) conditioned air (e.g., 20 °C and 50–60% humidity) renewed by laminar flow ventilation 3–5 times per hour and not returned;

(*b*) one-way flow for linen, equipment, beds, incubators, and bottles; everything entering the department should be autoclaved if possible;

(*c*) toilets outside the department.

7. *Bacteriological control*

(*a*) each newborn infant should remain in his own bacteriological microclimate;

(*b*) no tables for changing napkins; this should be done on the bed;

(*c*) individual overalls, changed for each child;

(*d*) high-pressure air (see 6);

(*e*) linen, etc. (see 6);

(*f*) special plumbing; basins and baths without safety overflow; exchangeable interceptors, changed every month.

8. *Equipment of each workplace*

(*a*) oxygen, air, vacuum if required;

(*b*) 8–10 electric points;

(*c*) facilities for electronic surveillance (problem of earthing for stabilization of current, etc.);

(*d*) lighting at each workplace;

(*e*) general lighting sufficient to identify icterus and cyanosis.

9. *Adjacent premises*

(*a*) surgical ward;

(*b*) laboratory (blood gases, etc.);

(*c*) central observation unit;

(*d*) rest room for nurses;

(*e*) bottle store;

(*f*) general store and radiology equipment;

(*g*) cleaning room.

Outside the unit:

(*h*) toilets;

(*i*) cleaners' room;

(*j*) entrance hall;

(*k*) doctors' offices.

10. *Space*

(*a*) each area for intensive care: 8–10 m^2;

(*b*) each incubator: 2.5 m^2;

(*c*) each cradle or bed for before-term infants: 4 m^2;

(*d*) each bed for sick infants: 6 m^2.

The annex and service area should be double the area set aside for beds.

Space requirements for a unit of 40 beds:

4 intensive care areas:	4×10 $m^2 = 40$ m^2
10 incubators for newborn under 2000 g:	10×2.5 $m^2 = 25$ m^2
10 cradles or beds for newborn under 2000 g, transferred from incubators:	10×4 $m^2 = 40$ m^2

16 beds for newborn over 2000 g:		$16 \times 6\ m^2 = 96\ m^2$
Total space for 40 beds:	$200\ m^2$	
Annex and services	$400\ m^2$	
Total	$600\ m^2$	

11. *Staff*

Doctors: 4 to provide coverage 24 hours a day, all trained in resuscitation;
Qualified nurses: one nurse per bed;
Service staff: 6 (3 in the unit and 3 outside).

12. *Communications*

(*a*) telephone, internal telephone (emergency call system);
(*b*) windows between all rooms;
(*c*) telex between laboratory and unit;
(*d*) pneumatic tube (possibly);
(*e*) television, depending on arrangement of premises.

13. *Safety measures*

(*a*) Emergency exit;
(*b*) fire-fighting equipment; equipment for dealing with short-circuits.

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